BRAIN.

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ON HEPATO-LENTICULAR DEGENERATION, WITH THE ACCOUNT OF A CASE AND THE PATHOLOGICAL FINDINGS.

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INTRODUCTION.

THE Danish neurologist, Hall, in a recent comprehensive monograph [1], has collected from the world's literature twenty-three cases, with autopsy reports, in which a specific organic disease of the central nervous system has existed together with a profound hepatic cirrhosis and has included a detailed study of forty-five other cases, in which, from analogy with the cases proved by autopsy, this extraordinary combination was also, in all probability, present. Previous to the publication of this monograph, cases presenting this rare, double-sided pathological picture have been diagnosed either as progressive lenticular degeneration (first recognized and described by S. A. K. Wilson), as pseudo-sclerosis (described clinically by Westphal and Strümpell, and pathologically by Altzheimer), or as torsion spasm (first described by Thomalla). Clinically, all these diseases are characterized by varying degrees of diffuse muscular rigidity, together with involuntary movements. They develop no paralysis nor sensory changes. They show a strong tendency to be familial and hereditary. Pathologically they reveal an intense hepatic cirrhosis, which in the very large majority of cases gives rise to no symptoms during life, and a varying degree of destruction of one or all of the components of the corpus striatum, together with diffuse degenerative changes of a much less severe type in many parts of the brain.

One of Hall's main theses in his monograph is that, in spite of the fact that there are many secondary points of difference in the clinical

and pathological aspects of these three conditions, we are justified from their obvious general similarity in grouping them together under one term. One cannot disagree with this conclusion, which is amply justified by the rare combination common to all three diseases; and the grouping together of these three diseases is, moreover, a necessary step to take in the fuller elucidation of their unknown pathological cause, for many cases fit but awkwardly into any one of the three groups, and are, when critically examined, obviously transition types.

The case about to be described illustrates these points clearly. It will be seen that we are not justified in describing it as a clearly-cut example of Wilson's disease, or of pseudo-sclerosis, and it bore little clinical resemblance to torsion spasm. I have, therefore, described it under Hall's title of "hepato-lenticular degeneration," believing with Hall that the differences, from all points of view, between progressive lenticular degeneration of Wilson and pseudo-sclerosis of Westphal, Strümpell, and Altzheimer, are quantitative only.

A sign which appears in many of these cases is corneal pigmentation. From the published descriptions this is striking enough when specially looked for; it is due to the presence of brownish-black particles deposited in the membrane of Descemet, forming a pigmented ring about 2 mm. wide, and often only seen clearly by oblique illumination. There seems little doubt that it is found very frequently if carefully searched for. The case to be described, which was under observation for a week only, was not examined for this sign, but as we were unaware at the time of the delicacy of the pigment ring, no importance can be attached to this negative finding.

Case Report.

I. U., a schoolgirl, aged 12½, was admitted to the General Hospital, Bristol, under the care of Dr. J. O. Symes, on March 11, 1922, and died on March 20, 1922.

History.—The child was normal in every respect until the age of 8. About this time she had a succession of illnesses—measles, diphtheria, and scarlet fever, and the parents state that she afterwards became delicate and needed a great deal of care. At the age of 8 she could read and write as well as other children of her age, and she had learnt to knit well. After she had recovered from these illnesses, the parents kept her from school for some time (about six months), and they noticed then that she was "rather babyish." They attributed this to the long stay at home. On returning to school she progressed very slowly. The teachers on several occasions told the mother that they "couldn't make her out," and at the age of 10 the mother found that she

was "no good at anything she had to do with her hands"; for example, she had now to help her to dress, her writing deteriorated, and she could not knit as well as she could at the age of 8 years. The mother still attributing this to the child's long absence from school, says she "needed a lot of spoiling," and she found that other children were "making fun of her." From this time onwards the mother appears to have shielded and petted her in every way. She was an only child and was very sensitive of her inability to progress at school and of the awkwardness of her hands. The mother accompanied her everywhere; she ceased to play much with other children. Careful questioning regarding her general condition at this time elicited the facts that in spite of her slow progress at school the child was mentally alert, affectionate and trustworthy; she took her food well and slept well. This was her general state until a year before her death. At this time the mother noticed that often during the course of a day she had difficulty in understanding what the child said to her. She describes her speech as being "thick." At the same time she seemed to become "much more delicate" again. Her appetite became capricious, she was distressed about her school work and clung more to her mother. Very soon after this it was noticed that she had difficulty in holding things in her hands. Writing and knitting became impossible because of the "awkwardness" of her hands and she had difficulty in feeding herself. The first occasion in which this latter symptom was noticed was when late for school one morning she was attempting to eat her breakfast. The mother then noticed her hands shaking. She thought the child was nervous. The disability steadily increased. One doctor told the mother that the thick speech was due to adenoids, another, that the movements of the hands were due to chorea, and a third, that the child was "being spoiled" and was "getting too much sympathy." In spite of this, and realizing that the speech defect and awkwardness of the hands were progressing, and the child was always ailing in some respect, the mother decided to keep her at home. At this time she was in the third standard at school. She never again attended school. About May, 1921, the mother noticed that when out walking the child had developed a stoop. She scolded her for it, but says that "she stooped more and more and always held her hands up to her face." About this time the involuntary movements of the hands became very obvious, and the child developed a habit of holding her mouth slightly open, with the upper teeth "sticking out." About the time this change in facial expression was noticed the mother found that the child was always salivating. Her recollection of this is very vivid, as the child made her clothes so wet. The movements of the hands, the stoop, the altered facial expression, and the position in which the hands were held, made her extremely self-conscious if out of the house, and the mother says they came to an agreement that the child should walk behind her when they were in the streets. The child's disposition now began to change, she became irritable and restless, and had attacks of loud screaming. She developed a very marked "unsteadiness in her legs." During November, 1921, she had three attacks of copious epistaxis at intervals

of a few days. All the symptoms noted above, except the epistaxis, which never occurred again, now became very obvious, and in December, 1921, she was kept in bed, chiefly because of the unsteadiness in walking. Here the greatest difficulty seemed to be in feeding herself: it was difficult for her to pick the food from the plate, she always spilled some on the floor in the attempt, and in conveying it to her mouth she lost most of it over her clothes. She was so self-conscious of her disability that she preferred to eat alone, and her mother states that "the cat had most of her food."

Most of her symptoms at this time were liable to intermissions. For a few hours at a time the movements of the hands seemed to be under control, and her speech would be fairly intelligible. When out of bed, the stoop was now extreme, and her head used to "shake in all directions." She was often noticed to make grimaces, twisting her face up, screwing up her eyes, and her mouth was often "drawn up." The mother describes a symptom, noticed first about February, 1922, which was also observed during her short stay in hospital; when out of bed she would often "dance about in the room all huddled up." From the description it appeared that in an attitude of extreme flexion she would dance in circles, lifting her feet high from the ground and "working herself up," would get very excited and often fall. During February the mother found her in the bedroom lying on the floor. She could not explain how she got there, and appeared to be "dazed." Following this she was never left alone, and on three occasions the mother says she had "convulsions," and on many occasions "choking attacks." The "convulsions" lasted about two minutes. Her arms were involved in violent tremors, her head was bent stiffly backwards, her eyes rolled from side to side, and her face "worked dreadfully." During these attacks her mouth was widely open, and she made a choking noise in her throat. On recovering she seemed to be oblivious of what had happened to her. The "choking attacks" seemed to be of the same nature, always accompanied by a marked increase in the tremor, which became almost violent, and by facial spasms. At the end of February, 1922, she had a "seizure" which lasted one and half hours; this seems to have been a prolonged attack of what the mother previously described as "convulsions." Her mother at this time described her as needing constant attention. She could do nothing for herself, and had long attacks of screaming.

Family history.—The patient was the only surviving child. A sister died in 1911 at the age of 6 years 9 months, after an illness of four months. The family doctor states that this child had ascites, an enlarged liver and heart disease. The mother is only clear on two points—that much fluid was removed from the abdomen, and that the child's face and extremities were very blue. She does not appear to have suffered from any speech defect, from difficulty in walking, or involuntary movements. Her death was certified as due to tubercular peritonitis. No post-mortem examination was performed. The maternal grandmother is still alive, the maternal grandfather was killed in an accident. The mother herself is one of eight healthy children. On the father's side, there is no history of anything suggesting that any similar case has occured in his family.

Condition on admission.—On admission the patient was found to be well-nourished, and understood all that was said to her. When undisturbed she lay quietly in bed, generally in an attitude of semi-flexion, occasionally with the lower limbs extended, and generally showing no involuntary movements. Her face was flushed, and described as being often "twisted into a vacant grin." As soon as she was approached and spoken to, all her limbs immediately became forcibly flexed and adducted. ("She shut up like a knife.") Both thighs would flex on the abdomen, and the legs at the knees. The elbows were acutely flexed and the arms adducted, the fingers being firmly clenched into the palms. The limbs were rigidly held in this position, the elbows resting on the knees; and when thus rigid, the hands and arms and the feet and legs were involved in a coarse rhythmical tremor of about four oscillations per second. The tremor was occasionally absent in the rigid legs, but always present in the arms when they were rigid. This attitude would be maintained for some minutes. It was difficult to straighten the rigid limbs and fingers, but after a time the tremor would partially cease, and the limbs could be brought to a position of semi-extension. Whilst being examined, neither rigidity nor tremor was entirely absent.

When told to move her limbs she always attempted the movement, but was generally frustrated by increased rigidity and coarse clonic movements of the limbs she was attempting to use. Simple observation, and especially any emotion, invariably accentuated the rigidity and tremor.

She had a very marked speech defect, which in common with her other symptoms was liable to intermissions, when it showed definite improvement, improving as the general muscular rigidity lessened. When she was excited or under examination her speech was limited to "yes" or "no" and short monosyllables, and her attempts to construct sentences resulted in the rapid articulation in short bursts of unintelligible sounds, with a decided nasal tone. Generally, if not harassed, she could frame short sentences of short words, but the same nasal tone was present; the words seemed to be forcibly projected one by one in rapid succession against resistance. Attempts at speech, especially if unsuccessful, increased the facial spasm, and her inability to converse caused her great distress.

Although regarded as excitable and on one occasion as hysterical, she was not very lachrymose. She cried, however, if forced against her will to perform any co-ordinated muscular movements other than walking. She attempted to obey simple commands, but generally failed if they involved any co-ordinated muscular action. The command "Turn your eyes to the right" was obeyed by a momentary flicker only of both eyes in the required direction. When told to move her rigid limbs, she generally attempted the movement slowly and laboriously, but never completed it, and showed distress and confusion at her inability to do so.

On admission her pulse rate was 136, and temperature 101° F. The temperature fell and oscillated between 98° F. and 99° F. during the nine days she was in hospital, but the frequency of the pulse (100 to 120) was maintained until her death.

No abnormality was found in the organs of the thorax. The liver dullness extended from the sixth rib to ½ in. above the costal margin in the mid-clavicular line. Neither abdominal tenderness nor free fluid was found, and no abdominal viscus was felt.

On the day of admission the urine contained a trace of albumen (0·025 per cent.). It was otherwise normal, and albuminuria was never detected again.

Nervous system.—In addition to the emotionalism, the memory was considered to be slightly impaired. There was no suggestion of drowsiness, delirium, hallucinations nor delusions, but at times she was said to be "slightly imbecilic." This was, certainly, largely due to her dysarthria.

Involuntary movements were present, as described above. They were generally most marked in the right lower limb.

There was no apparent loss of visual acuity, the corneæ were normal, but the fine pigmentation, only clearly visible by oblique illumination, recently described in this disease was not looked for. The pupils were equal and round, and their reactions normal. All external ocular movements were possible, but there was a definite inability to retain the eyes in any fixed position of conjugate deviation. There was no nystagmus. There was no loss of sensation in the skin of the head and neck. The movements of the facial muscles were equal. Auditory acuity was normal. She had some difficulty in swallowing solids, none in swallowing fluids. All movements of the sterno-mastoid, trapezius and lingual muscles were possible, but uncontrolled and jerky, and as in the limbs contraction was followed by some rigidity.

Sensory functions.—There was no complaint of pain, headache, vertigo nor tingling, and no impairment of sensation found.

Motor functions.—There was no paralysis or paresis, but a striking inability to perform any co-ordinated muscular act. She was occasionally observed to show no abnormality when lying in bed, but if she sat up or attempted to stand, her whole musculature stiffened and her limbs became involved in tremor. This happened also almost immediately she was conscious of being observed, and could never be entirely abolished whilst under examination. Her movements of general flexion ("shutting up like a knife") on being approached and during examination are described above. It was repeatedly observed that the diffuse muscular rigidity and tremor could be greatly lessened, apparently at will, but they could never be abolished while the child was sitting or standing. The intensity of both these symptoms was liable to very marked intermissions, and a definite improvement was noticed even during her tragically short stay of ten days in hospital.

Her attempts at walking varied greatly. When first admitted, attempts at walking under observation resulted in nothing more than a series of grotesque, purposeless movements. If raised from the attitude of flexion, which during her first few days in hospital she generally adopted when being examined, she seemed unable to get her feet on the floor, and had to be half carried and half supported before she could place them on the ground. Her muscular rigidity

at this stage was intense, and her whole musculature involved in tremor. In an attitude of flexion, she attempted to walk by first holding to the nearest support, and then, after considerable hesitation, she would rapidly and forcibly raise one foot high from the ground and just as rapidly bring it down again. This movement was quickly followed by a similar movement of the other foot. The feet were raised apparently by a single explosive contraction of the thigh muscles, and the rigid lower limb was raised, as it were, in one piece, with the ankle-joint fixed. The result of these movements was that she succeeded in gyrating in incomplete circles about her point of support. Owing to their sudden jerky character these movements were described as being "like those of a mechanical doll propelled by strings," and the gyration as being reminiscent of a "dancing monkey." An attempt to make her walk after she had been in hospital a few days showed that she had improved considerably. The rigidity and tremor again appeared when she sat on the edge of the bed, so much so that her feet had to be forcibly placed on the ground and held there before she could get up. Her attitude on standing was less flexed and the tremor less generalized. After a latent period she suddenly and forcibly made three rapid and very uncertain short steps forwards, sprawling on completing them, and would have fallen forwards if not supported. About the same time she succeeded in reaching the lavatory, a distance of twelve yards, by pushing a chair in front of her. The arms, and often the legs during walking, were constantly tremulous, and now and then thrown into clonic contractions. It was repeatedly observed that tremor and clonic contraction were practically absent until some attempt was made to perform a co-ordinated muscular action (e.g., standing) and that rigidity was thereby increased. The hand grips were powerful and equal, but unsustained.

Reflexes.—The conjunctival, epigastric and hypogastric reflexes were present, brisk and equal. Both knee-jerks were present; they were equal and not exaggerated. The plantar reflex was flexor. The ankle, wrist and elbow jerks were brisk and equal. There was no ankle clonus. It was difficult to decide if Kernig's sign was present. There was no incontinence. There were no tropic lesions of skin or bones. The feet tended to assume a position of slight equino-varus, which could be easily corrected. It was more marked on the left side. The vertebral column was normal.

Sympathetic system.—The pupils dilated to shade and there was no proptosis, exophthalmos, nor lid retraction.

Course.—Very little change took place in her condition for four or five days after admission. Following this, a decided diminution was noticed in the tremor, and the range of voluntary movement increased.

At 1 a.m. on March 20, 1922, without any apparent premonitory symptoms, she had a series of about fifty convulsions, accompanied by violent twitching of the face and limbs. These convulsions continued almost uninterruptedly for five and three-quarter hours, she vomited incessantly, the pulse was very frequent and there was hyperpyrexia (temperature at 4 a.m. 108·2°). At first the face was flushed and red, but she gradually became cyanosed, mucus

accumulated in the upper air passages, and respiration failed five and three-quarter hours after the commencement of the attacks.

Post-mortem examination (performed 7½ hours after death).—The body was that of a well-nourished child, showing no evidence of retarded development, and no abnormality externally. There was certainly no wasting of muscles and the body was well covered. The muscles were all flaccid. Nothing abnormal was found in the tongue, tonsils, or pharynx, but the larynx and trachea contained much frothy mucus. No abnormality was detected in the œsophagus. The thyroid was normal to the naked eye. No disease beyond an acute terminal pulmonary œdema was found in the contents of the thorax. There was about a pint of clear fluid in the flanks, but no adhesions or distention of the bowel. The edge of the liver was above the costal margin. No abnormality was discovered in the stomach, duodenum, small bowel, or extra-hepatic biliary system. No glandular enlargement was found. There was some congestion and thickening of the cæcum and ascending colon, but the remainder of the large bowel was normal. The mucous membrane of the cæcum was reddened, and rather velvety, and three small spherical swellings about 2 mm. in diameter, attached by broad stalks to and projecting 2 to 3 mm. above its surface, were seen in its posterior wall. Four similar nodules were found in the rather thickened and congested mucous membrane of the ascending colon. The spleen was larger than normal (weight 160 grm., long axis 14½ cm.). Its capsule was unaltered, but the pulp was firm and rather resistant, and its section was flat and appeared to be rather fibrotic. The liver showed the typical gross picture of multilobular portal cirrhosis (weight 907 grm. —32 oz.). It was shrunken and considerably deformed, its edges were blunted and its general configuration tended to be spherical. (Greatest antero-posterior diameter 8 cm., greatest diameter from superior surface to lower edge 14·5 cm.). The whole surface was studded with irregularly-sized granulations, varying from 2 to 12 mm. in diameter, yellowish or yellowish-red in colour, separated from each other by deep red, shallow depressions, and here and there by steep fissures. The capsule showed general congestion, and a moderate degree of opacity and thickening. In places this thickening was more pronounced and bridged over the deeper fissures on the surface.

On section, a wide-meshed network of fibrous tissue was seen to divide the cut surface into circular and ovoid groups of lobules, 1 to 15 mm. in diameter; these islands of lobules were light yellow, and their lobular pattern obscured. The fibrous tissue was deep red and rather

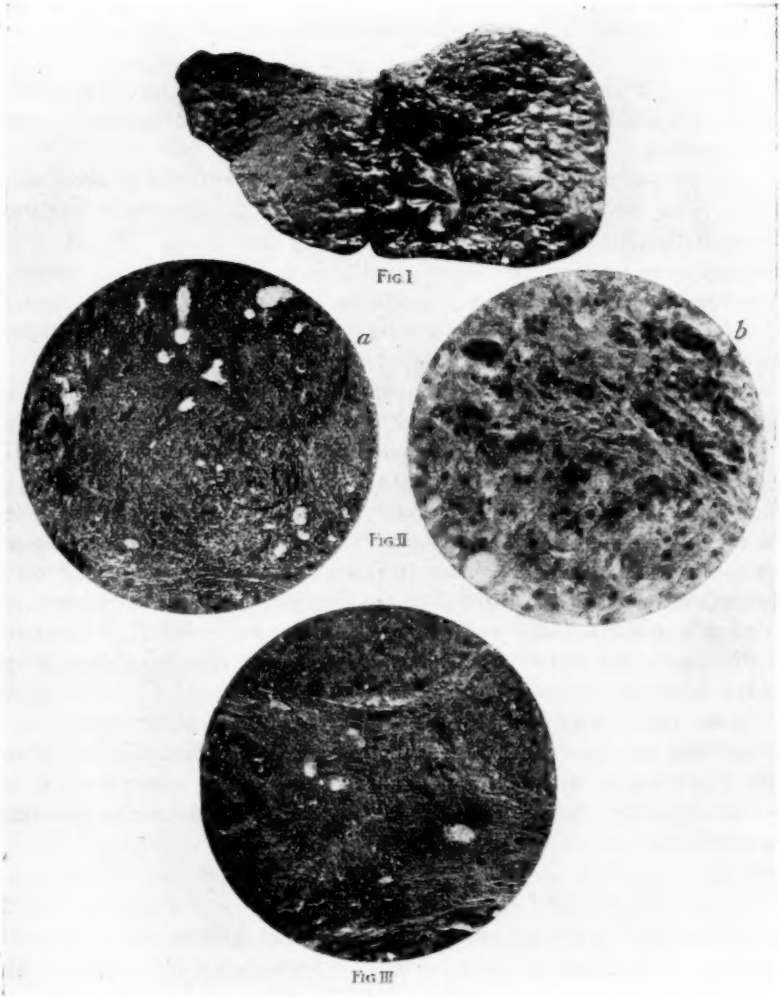


FIG. 1.—Liver; hepato-lenticular degeneration (¼ natural size).

FIG. 2—Photomicrographs of section of liver. *a*, Low power view showing lobule isolated by cirrhotic process. (Obj. Leitz, 3a.) *b*, Higher power view of portion included in circle in fig. 2*a*, showing proliferating bile-ducts at edge of a lobule. (Obj. Leitz, 6a.)

FIG. 3.—Photomicrograph of section of liver. Low magnification view showing broad band of cellular, vascular tissue isolating groups of lobules. (Obj. Leitz, 3a, oc. × 8.)

translucent. No changes were seen in the intrahepatic bile-ducts, or in the portal vein and its main branches.

The pancreas, kidneys, suprarenals and genital apparatus were normal.

Brain.—There were no naked-eye signs of disease in the skull, dura mater, pia-arachnoid, venous sinuses or pituitary body; middle ears were normal.

The corpus callosum was divided by an antero-posterior incision, and a horizontal section made through each cerebral hemisphere, passing through the lowest points of the splenium and genu. No obvious changes were seen in the basal ganglia or in the ventricular system. A series of coronal sections was made on each side but no gross lesion was found in the central grey matter. The mid-brain, pons, medulla, cerebellum and spinal cord appeared normal.

After the brain had been hardened in formalin it was noticed, on comparing it with the normal brain of a child of the same age, that the usual outlines of the lenticular nuclei were partially lost and their colour a deeper yellow. On cutting the frontal lobe five or six foci were found, from $\frac{1}{4}$ to $\frac{1}{2}$ square cm. in area, especially about the frontal pole on each side, where the cortex looked thicker and appeared to be beset with minute cavities and dusted over with small brown dots and very delicate brown streaks. No naked-eye change was found in the rest of the brain, and this naked-eye change in the frontal cortex, in common with those in the lenticular nucleus, was only seen after careful scrutiny of the hardened brain.

The central nervous system (unfortunately partly spoiled by immediate section) was placed in 10 per cent. formol-saline, after selecting portions of the basal ganglia for alcohol and Zenker fixation, to be subsequently stained by the Nissl and Mallory neuroglia methods respectively.

Pathological Histology.

Technique: Central nervous system.—Four blocks cut in coronal section were obtained of the basal ganglia from each side. At the same time similar blocks were taken from the brain of a case of lobar pneumonia, in which death was preceded by high temperature. The two series were subsequently subjected to the same methods of staining, &c. From each block two thinner blocks were cut and fixed in alcohol for Nissl staining. The other blocks were fixed in formol-saline with the rest of the central nervous system. After fixation corresponding

pieces were taken from each brain and cut by the paraffin process and by freezing.

Sections were stained by the following methods :—

(1) By Goodpasture's methylene blue modification of Nissl's method.
(2) By hæmalum and eosin, and iron hæmatoxylin and van Gieson.
(3) By Lhermitte's neuroglial stain (modified).
(4) By Mallory's method for neuroglia.
(5) By scharlach R. and hæmalum.

Pieces were cut from all regions of the cerebral cortex, mid-brain, cerebellum and dentate nucleus, mid-pontine region, medulla and upper cervical cord, and treated according to the same technique. The rest of the material was put through the Kulchitsky-Pal process for myelin. Fixation of the material was considered satisfactory owing to the normal appearance of the red blood cells in all sections.

Paraffin and frozen sections were taken of several pieces of the liver and stained by methods (2) and (5) above. Paraffin sections of the cæcum, colon, mesenteric glands, spleen, pancreas and thyroid were also made.

Basal ganglia.—The corpus striatum presented very marked pathological changes, the putamen in all sections showing conspicuous diffuse degenerative disease of the bodies of its large nerve cells. No normal large nerve cells were seen in any sections, and the degeneration was of such a degree that extraneous factors, such as post-mortem autolysis and the conditions immediately preceding death, were judged to have played practically no part in its causation. After examining the series of sections cut from the putamen it was decided that, as far as its nerve cells were concerned, there was a definite selective atrophy of the large type of cell, that this process had spared many of the small nerve cells, and that degenerative changes in the small type of cell were much more recent and had not progressed as far as in the large cells. The changes seen in the large nerve cells varied. Here and there as many as ten large neuroglial nuclei, varying in form from circular to ovoid and staining weakly, were seen grouped together in a lacuna, over and under an unevenly-stained mass representing the ultimate stage of destruction of a large nerve cell, often hardly recognizable as such. This extreme change was not common, the neuronophagy usually being much less conspicuous, and the outlines of the necrotic cell distinguishable. Much more frequently were encountered very swollen cells with diffusely and irregularly stained cytoplasm, still showing indications of processes, but generally devoid of anything resembling a nucleus. Up to six pale and often irregularly shaped nuclei were present in the neighbourhood of these cells. Occasionally the nerve cell was shrunken

and collapsed, and fairly frequently the cell wreck appeared to be dusted over with coarse masses and marginally-placed powdery deposits of deeply-staining irregular granules. When a nucleus was found in such a cell it was at its edge, or partially extruded, and it stained deeply and appeared deflated.

Chromatolytic changes in the small nerve cells were less constant, and the proportion affected smaller. In no case had these changes progressed to the extreme stage found in the large nerve cells, but when present they were much more advanced than those in control specimens, and such alterations as could be attributed to post-mortem autolysis and the terminal events in the disease.

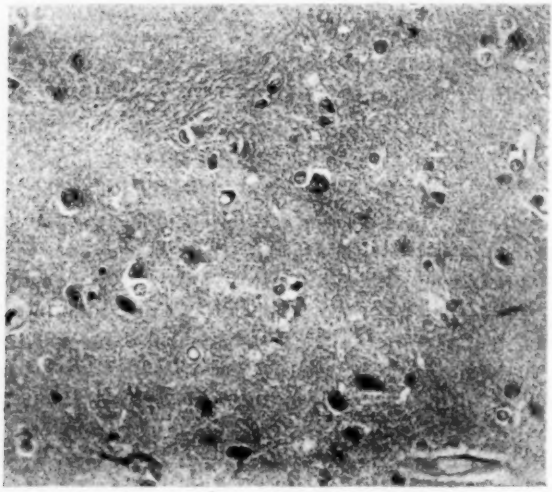


FIG. 4.—Photomicrograph of normal putamen. (Stain, iron-hæmatoxylin and van Gieson. Obj. Leitz, 6a.)

The putamen showed general and unmistakable gliosis. The number of neuroglial nuclei and the type of cell both gave clear indications of this change. The increased number of glial nuclei was hardly so striking as the change from the normal in the type of cell, cells with large clear nuclei being the predominating variety. As cell destruction was so much more common in the large type of cell, the increase in the number of, and change of type in the neuroglial cells, was really the most noticeable change observed before making a detailed examination under high magnification. The nuclei of these

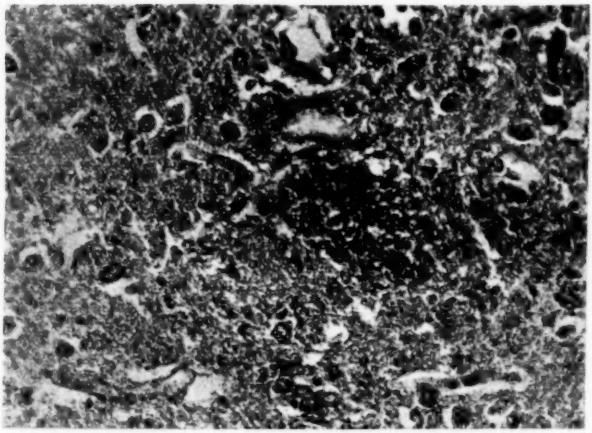


FIG. 5.—Photomicrograph of putamen in case described, under the same magnification and stained by same technique as the normal control (fig. 4). It shows increased density and sponginess of neuroglia, and many pathological glia cells.

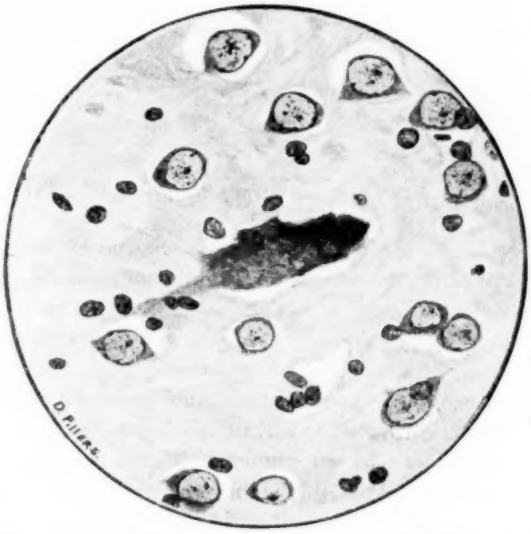


FIG. 6.—Putamen of case reported showing a necrotic nerve cell in centre of field. (Obj. Leitz, $\frac{1}{12}$a, oc. × 8.)

cells were large and clear, and stained faintly. Their shape varied from circular to bluntly spindle-shaped; some were bowed, others were slightly indented. A long search was made for the neuroglial giant cell described by Altzheimer as specific of the neurogliosis in pseudo-sclerosis; two doubtful examples of this type of cell were found, but in both instances it was difficult to distinguish between the neuronophagy occurring about a necrotic nerve cell, and a multinucleated cell. I experienced the difficulty, mentioned by Hall, of distinguishing between

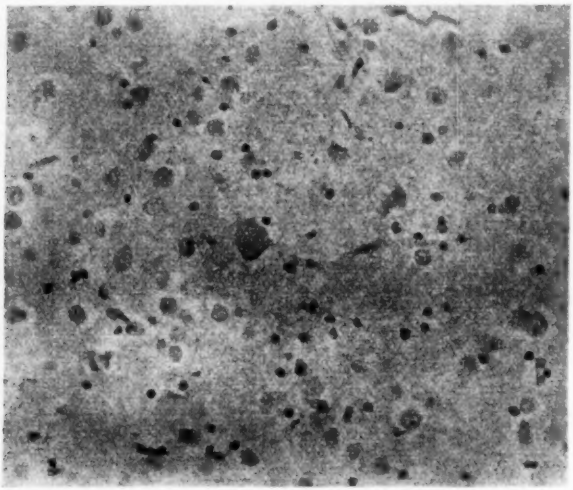


FIG. 7.—Photomicrograph of caudate nucleus in case reported. (Stained by polychrome blue, no counter-stain.) It shows large numbers of pathological glia cells, and one degenerated nerve cell in centre of field.

the small nerve cells of the putamen and pathological neuroglial cells, and relied chiefly on normal controls in assessing the degrees of proliferation of the latter. I could not demonstrate any neuroglial fibre formation in the putamen, and after staining many sections came to the conclusion that there was a considerable under-production of fibres by the cells, and in all probability a diffuse degenerative change in the supporting tissue, which by all connective tissue stains appeared gross, swollen and spongy-looking. No change recalling an inflammatory process, nor any disease nor alteration in the blood-vessels, were seen.

Caudate nucleus.—Diffuse and advanced degeneration of the bodies of the nerve cells was almost as constant in this nucleus as in the puta-

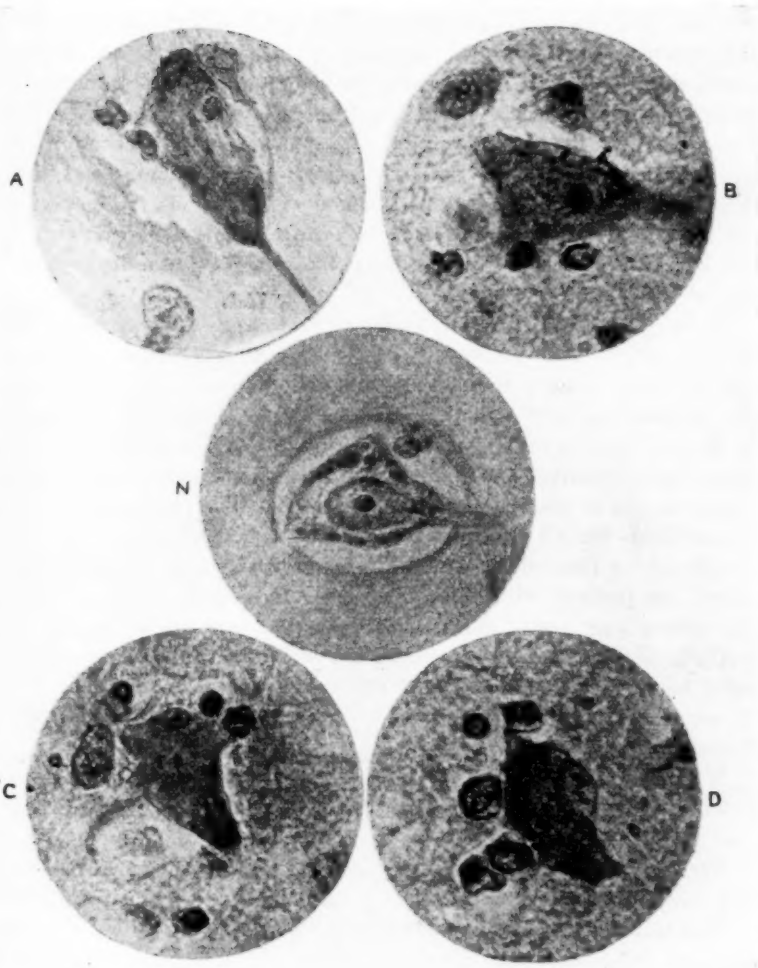


FIG. 8.—Photomicrograph of nerve cells from lenticular nucleus. (Stained by polychrome blue.) A and B from putamen; C and D from caudate nucleus; N from the putamen of a case of lobar pneumonia, dying with high temperature (normal control).

men. This was unlooked for at the outset of the investigation, but sections taken from all parts of the nucleus confirmed it. As in the putamen, the changes were diffuse, and there was no suggestion of focal lesions. On the whole, reduction of the cell bodies to shrunken masses was less noticeable than in the putamen, but the proportion of damaged cells was just as high. Neurogliosis was of the same degree as was found in the putamen. The impression left in one's mind after examining both nuclei was that the lesion in the putamen was somewhat older. In both the putamen and caudate nucleus, frozen sections did not show more than a few scattered granule cells staining by scharlach R., and the Virchow-Robin spaces were practically free of cells of this type.

Globus pallidus.—The nerve cells of both segments were singularly free from the extreme changes found in the caudate nucleus and putamen, but degenerative changes in the bodies of the large motor cells were generalized and diffuse. The commonest change consisted of swelling of the cell with excentricity of its nucleus, powdery marginally placed Nissl granules, and diffuse staining of the cytoplasm. Neurogliosis was not so marked as in the putamen. The change was obvious in most fields when examining this nucleus with a low power, but occasionally two or three fields would be encountered which demanded fairly critical comparison with normal controls to establish any alteration. The neurogliosis was of the same type as was found in the putamen.

Optic thalamus.—An occasional cell was found in sections showing slight degenerative changes, but hardly of a greater degree than would be accounted for by the mode of death. There was no definite neurogliosis.

No constant clearly-cut lesions were found in sections of the subthalamic nuclei, mesencephalic nuclei, or in the grey matter of the pons and medulla oblongata.

Cerebral cortex.—The small naked-eye foci showing increased thickness and a finely pitted appearance in the cerebral cortex of the frontal lobes in the formalin-hardened brain were very obvious under low magnification in stained specimens. All the pieces showing this change, selected from the frontal region, were difficult to prepare by the paraffin and freezing methods because of their increased friability. Under low powers these regions of the cortex showed a uniform gross abnormality, consisting of a prolific new-formation of well-developed blood-vessels occupying fairly accurately the area of cortex extending from the middle of the supraradiary layer to the junction of the grey and white matter.

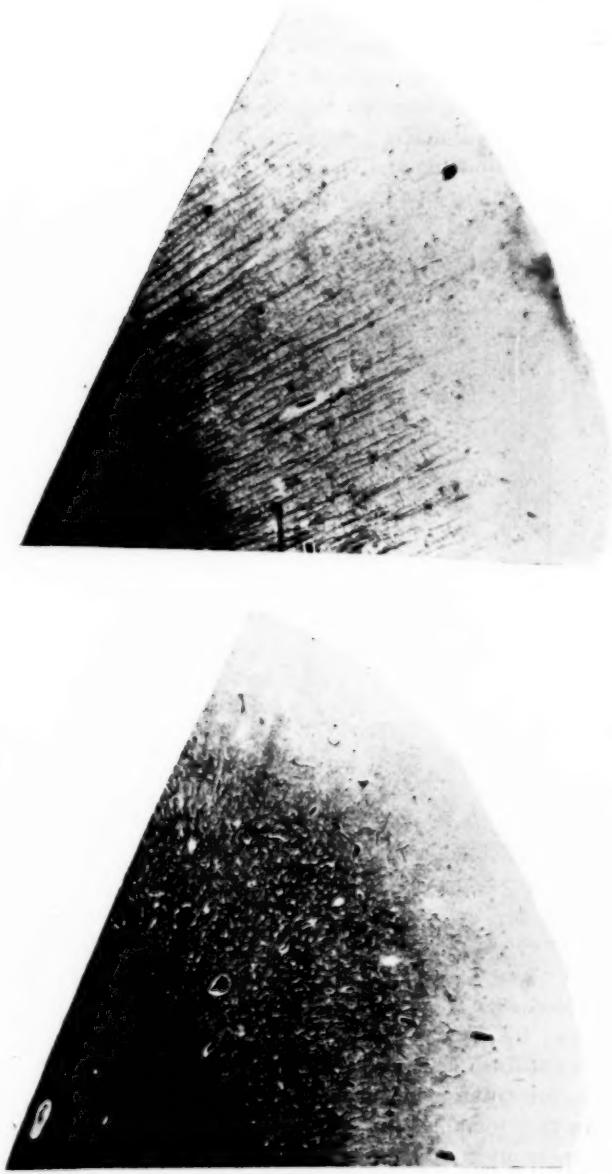


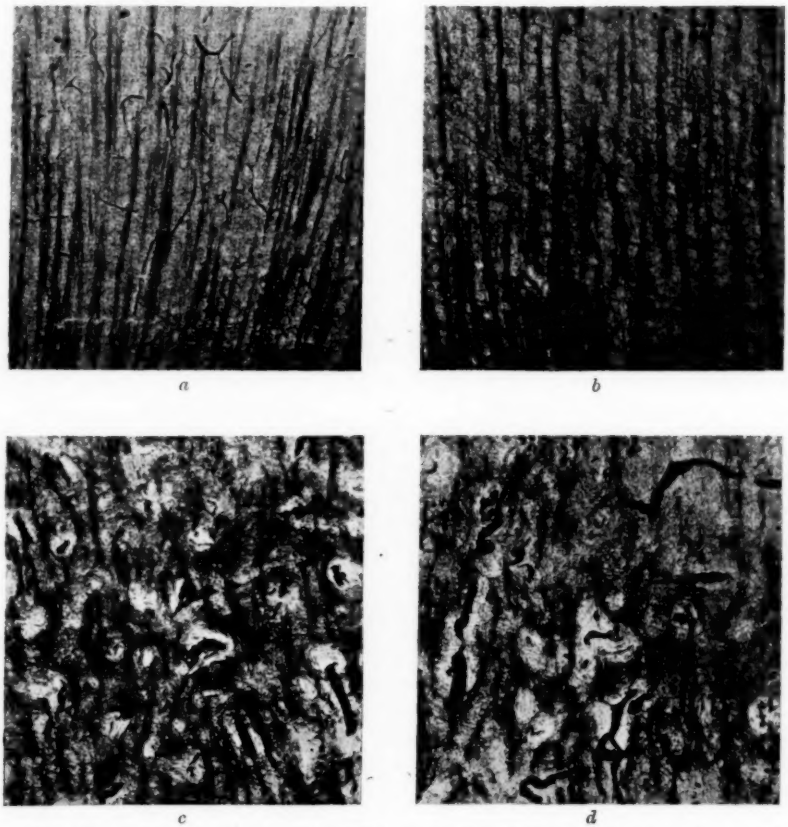
FIG. 9.—Photomicrograph of section of superior frontal gyrus. (Stained by Kultchitsky-Pal process.) The upper photograph was taken from the edge of a focus and is almost normal in appearance, the lower from a focus of vascular new formation.

In the radiary layer this vascular new formation was sufficiently developed to cause very considerable distortion, interruption and degeneration of the nerve fibre bundles of this layer, and to obscure the cyto-architecture to a marked degree. It was to this new formation that the naked-eye pitting and friability of sections of this part of the cortex were due. The small cavities were probably only exaggerations of the normal perivascular spaces around the larger of the newly-formed vessels.

FIG. 10.—Photomicrograph of a vertical section of the cortex of a frontal convolution. (Stained by the Kultchitsky-Pal process. Magnification × 14.) It shows a focus of vascular new-formation occupying the free surface of the convolution. The areas enclosed in numbered squares are represented under higher magnification in next figure.

The same change was found but to a much less extent in many parts of the cortex; the degree shown in figs. 9 and 10 existed only in the frontal cortex of both sides, especially in the anterior part about the frontal poles and in the anterior halves of the superior frontal gyri. Here the vessels were very tortuous and in thicker sections formed spirals, closed loops and knots often causing complete interruption of the larger nerve fibre bundles. There was no indication that the vascular new-formation was derived from the pia-arachnoid. It was accompanied by no inflam-

matory changes, and the walls of the vessels were so well formed and the vessels themselves appeared to be so well accommodated in the tissue that congestion and dilation of previously existing vessels could be definitely ruled out as a cause of the condition. The vessels were



a *b*

c *d*

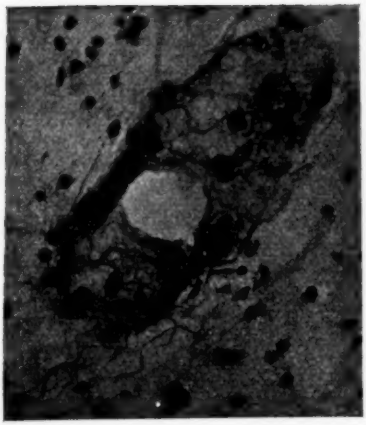
FIG. 11.—*a*, Normal control; Weigert-Pal preparation of the frontal cortex of a normal brain, but showing prominent vessels. *b*, Cortex included in area marked II in fig. 10, taken from the edge of the lesion. *c* and *d*, Cortex included in area marked III and IV in fig. 10, showing new-formation of vessels and interruption of the bundles of nerve fibres.

for the most part of the calibre of capillaries and pre-capillaries; most of the latter had a delicate well-formed elastic lamina and a single or double layer of muscle-cells. Some vessels of the calibre of pre-capillaries contained no elastic tissue in their walls, and in a considerable

number of these the lumen was very considerably reduced by thickening, corrugation and infolding of the vessel-wall. In some the thickening of the wall was due to hyperplasia of muscle-cells, but in the majority it appeared to be a result of a rich investment of the wall by a closely-set and abnormally rich neuroglial network (see fig. 12, *a*). In no sections were the vessels dilated; the majority contained blood-cells, and no thrombosis was seen. The perivascular spaces around the vessels were large and roomy. It was exceptional for any vessel to fill its space completely, which was generally empty except for two or three "granule cells" containing lipoid granules. The abnormally roomy perivascular spaces were almost as prominent in frozen as in paraffin sections, and, owing to the tortuosity and frequent branching of the vessels they contained, a general view under low magnification gave the impression of many branching linear cavities containing central vessels, lying at all angles to each other, and separated by diffusely and deeply stained, yet richly cellular supporting tissue. There was no evidence that the cavitation was due to any other factor than this, for although the parenchyma was considerably altered it showed no gross softening nor intrinsic cavitation.

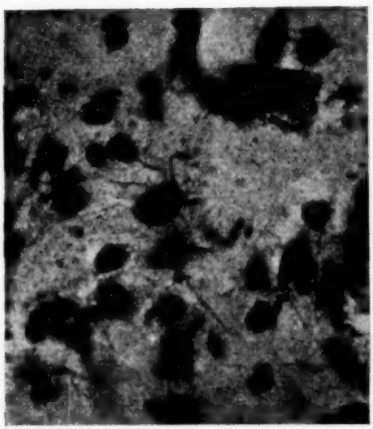
The vascular new-formation spread for a short distance only into the white matter, and was generally most intense at the summit of the convolution, the cortex lining the floor being often quite free from the change. It was peculiarly localized, the free surface of one convolution would show the change over an area not exceeding one square centimetre, the neighbouring one would show the same change over a similiarly sized area, but at a distance of 3 or 4 cm. away. These lesions were bilateral and most marked in the frontal lobes, being present on their superior, anterior, and antero-inferior surfaces; they were not, however, rigidly symmetrical, the foci on each side being scattered apparently at random over the surface. The extreme change in the frontal lobes apparent on naked-eye examination in the formalin-hardened brain was not visible elsewhere, but in sections taken from other regions a milder degree of the same changes was fairly frequently seen. In no case was this sufficient to cause the same gross nerve-fibre degeneration nor deformity of the cell-layers.

Where the affection was most marked, the supporting and nervous tissue showed striking changes. The neuroglia in its staining reactions was very similar to that found in the putamen—coarse, diffusely-staining and cellular. It contained a moderate number of the same large fibre-free glial cells as were found in the putamen,



a

b



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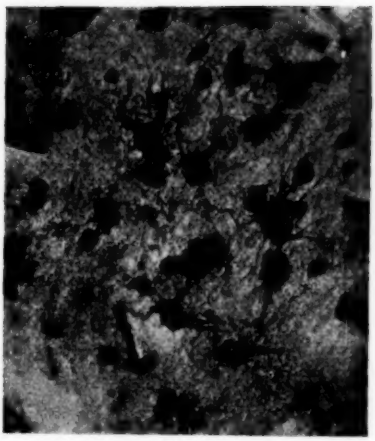

d

FIG. 12.—Photomicrographs of sections of the frontal cortex through a lesion similar to that shown in figs. 9 and 10, stained by Lhermitte's method for neuroglial fibres. *a* Shows neuroglial investment of the wall of a newly-formed vessel; *b* shows spider-cells in close relation with the wall of the vessel; *c* and *d* show large type of fibre-forming glia cells found in large numbers in the cortical foci.

but there were in addition considerable numbers of large fibre-forming glial cells, especially where the vessels were most numerous. (See fig. 12, *b*, *c* and *d*.) The same difficulty was found in distinguishing large glial cells from small nerve cells, but by comparison with normal controls it appeared certain that the cell increase in these cortical foci was due to the presence of pathological neuroglia.

FIG. 13.—Photomicrograph of section of a cortical focus similar to that shown in figs. 9 and 10. Note the new formation of vessels. (Obj. Leitz, 3a, oc. × 8.)

Degeneration of the cortical cells was confined to the areas where the vascular new-formation was present. Here it was considerable and had affected an appreciable number of the medium and large pyramidal cells. Much of this cell degeneration must be ascribed to the distortion and degeneration of the fibre bundles, caused by the prolific vascular new-formation, since the Weigert-Pal preparations showed a marked degree of fibre degeneration. In both layers of large pyramidal cells all the extreme grades of degeneration were present and satellitosis was established. Loss of nucleus, shrinking and diffuse deep staining of the cell-body were the commonest changes. There was no doubt, however, that compared with the cell degeneration in the striate body the process was much less uniform, and some pyramidal cells, especially at the edge of the cortical foci, had escaped, whilst a considerable number of the small pyramidal cells were intact.

Cerebellum.—No definite lesions were found in the cerebellar cortex. The majority of the cells of the dentate nuclei presented degenerative changes consisting of shrinking and atrophy of the cell-body and deep

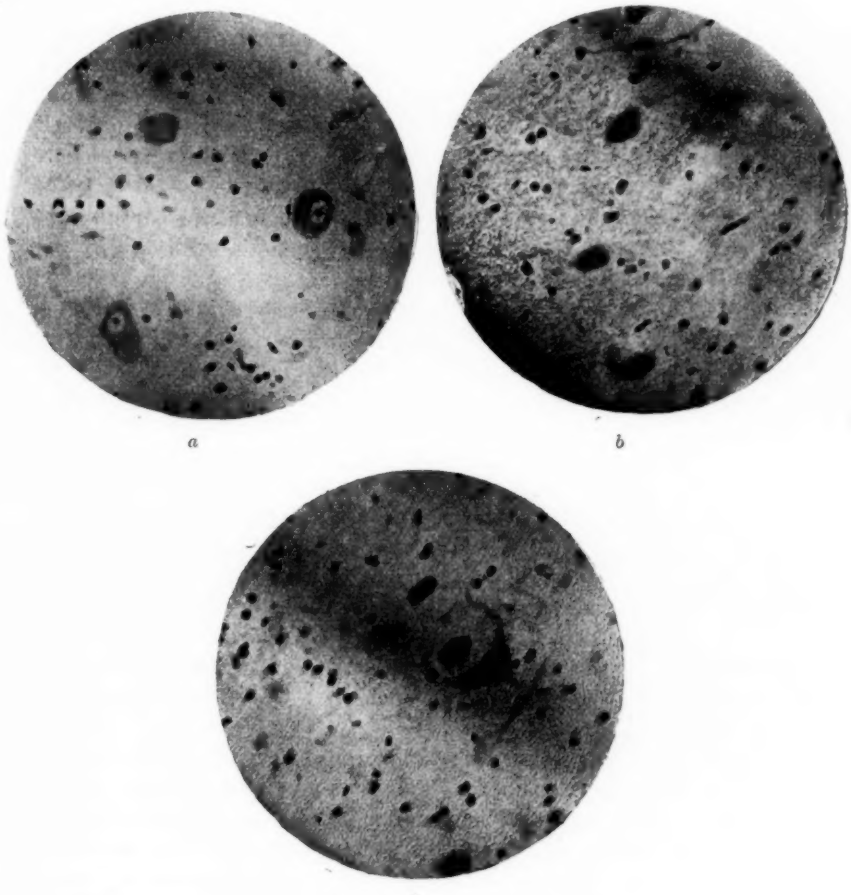

FIG. 14.—*a*, Photomicrograph of a normal dentate nucleus, stained by polychrome blue; *b* and *c*, dentate nucleus in case reported, showing two groups of degenerated nerve-cells. (Technique and magnification as in the normal control.)

staining of the cytoplasm. There was mild neurogliosis in the nuclei, but no gross lesion such as was found in the putamen of the lenticular nucleus.

Subthalamic fibre system.—Many factors contributed to make this examination unsatisfactory, the chief being the fact that at the autopsy this region was cut in many places, making it impossible to orientate the pieces afterwards. However, a few sections were obtained which showed definite and well-marked degeneration of the fibres of the ansa lenticularis. The change was gross and shown well by the Weigert-Pal method. Dr. Blachford, of the Bristol Mental Hospital, gave me considerable help in the anatomical localization of the degeneration, and expressed complete agreement with this diagnosis.

Liver.—The naked-eye appearances of multilobular cirrhosis were confirmed microscopically. A wide-meshed network of fibrous tissue was seen to enclose in its meshes groups of three to eight liver lobules. This cirrhotic process had the following salient characters:—

(*a*) It was excessively vascular.

(*b*) It showed no tendency to invade the isolated lobules except at their extreme edges.

(*c*) It was composed of broad sheets of rather immature fibrous tissue, lying in which were: (1) A prolific new-formation of bile capillaries, and (2) many foci of mononuclear cells tending to be disposed in relation to the walls of the numerous vessels.

The liver cells of those lobules in the centre of the isolated groups of lobules were normal, except for recent venous congestion, and little change was found in the more peripheral lobules, except towards their edges. Here the fibrosis had cut off and isolated groups and columns of liver cells, and very occasionally had completely isolated a lobule. The cells of these isolated lobules and groups showed all pathological changes from moderate fatty infiltration (with single droplets and an eccentric normal nucleus) to the changes associated with cell-death.

As the number of isolated single lobules was small, and the isolation of cell groups not conspicuous, the amount of actual destruction of the hepatic parenchyma was not large. The increased vascularity of the fibrous tissue was due to the presence of enormous numbers of widely-open, thin-walled fragile vessels, which were confined to this tissue, and, like it, showed no invasion of, nor connection with the hepatic lobules. They were generally lined by a double layer of endothelium, were devoid of an elastic lamina, and the muscle was either absent or very scanty. The fibrous tissue itself was obscured by them, but it appeared to be much more mature and of older date, especially at the edges of the lobules. Toward the centre of the cirrhotic bands

it was less mature. The bile capillaries were numerous, and their epithelium actively growing. They showed little tendency to invade the lobules, or to fuse with the more or less isolated liver cells lying in the cirrhotic tissue. No bile stasis was seen in them.

The collections of mononuclear cells appeared to lie in foci within the fibrous tissue. In some parts they were few, in others a rich infiltration of the tissue was present. They were constantly most numerous around the thin-walled vessels, and immediately surrounding the vessels a fairly high percentage of them were polynuclear. Others were typical plasma cells, and at the edges of these cell collections the majority were typical lymphocytes.

Sections of the liver stained by Gram's method showed no organisms, and no result was obtained in sections stained for pathological pigmentation.

Colon.—Cultures were made from the cæcum, the transverse colon, the descending colon and the mucous membrane of the ascending colon. No pathogenic organisms were isolated.

The nodules in the cæcal wall consisted of polypoid projections of hyperæmic inflamed mucous membrane, overlying a somewhat fibrotic submucosa. There was no gross loss of mucous membrane in any section, but the glands in all sections were widely separated by an abnormally rich cell-exudate. This was true of all sections taken of the mucous membrane, as far as the splenic flexure, but it was most noticeable in the cæcum. Here and there were microscopic patches in the mucosa devoid of gland tissue, which was replaced by hyperæmic cellular tissue, in which a few groups of epithelial cells, the remains of gland-tubules, lay. The cells were chiefly of the large mononuclear type, lymphocytes were not conspicuous, but polymorphonuclears were fairly numerous. These microscopic gaps in the mucous membrane were numerous, and, taken together, represented a considerable loss of surface.

Although hyperæmia was prominent in these foci, no constant perivascular arrangement of the cell-exudate nor thrombosis of vessels was seen, and the fixed connective tissue reaction was not marked. Below these small breaches of surface, the muscularis mucosæ was pierced by the cell-exudate, but this did not extend far into the submucous coat which, on the whole, together with the other coats of the bowel wall, appeared normal. The lesion was regarded as a widespread subacute catarrhal colitis.

Summary of Case.

A girl, aged 12½ years at the time of her death, was noticed at the age of 10 to be awkward with her hands in writing and knitting, having been previous to this in all respects a normal child. This disability progressed slowly, and her speech became indistinct. She developed a stoop, a change in facial expression, excessive salivation, and a gross speech defect. Her motor disability progressed, and she developed coarse tremor of both upper limbs. At the age of 12 she could hardly walk, strangers could not understand her speech, and the tremor of the hands made it difficult for her to feed herself. During the last six months of her life all her symptoms became rapidly worse. She developed intermittent facial spasms, a gross speech defect, and a diffuse rigidity of her voluntary musculature, which made walking, sitting and standing almost impossible. These symptoms varied in intensity and she became subject to convulsions. She died two and half years following the onset of the disease, after a series of epileptiform convulsions lasting several hours.

Clinical examination revealed a diffuse muscular rigidity, affecting agonists and antagonists equally, which was increased by any attempt at co-ordinate muscular contraction and by emotion, but subject to intermissions during which its intensity lessened considerably. Associated with the rigidity, and increasing and decreasing with it in intensity, there was a coarse tremor of all four limbs. Attempts at walking resulted in a series of grotesque, disordered movements, in which she contracted all her muscles, but failed to accomplish the act. She had a marked degree of dysarthria. She was not paralysed, and had no sensory changes.

On post-mortem examination she was found to have an intense multilobular hepatic cirrhosis. The central nervous system showed no naked-eye changes, but microscopically the lenticular nucleus presented widespread degeneration of its nerve cells, and replacement of its supporting tissue by neuroglial cells of a pathological type which formed no fibres. This change was bilateral, and of equal intensity on the two sides. There were degenerative changes in the ansa lenticularis. The cortex of the frontal lobes showed foci just visible to the naked eye, in which a prolific vascular new-formation, nerve-fibre degeneration, and a considerable degree of nerve cell destruction were present. The nerve cells of the dentate nuclei were degenerated.

Discussion.

The case reported bears a strong clinical resemblance to Wilson's disease, showing most of its essential positive features; yet the pathological examination, especially the striking absence of naked-eye changes in the brain, is in favour of classifying the case as one of pseudo-sclerosis. This is brought out clearly by tabulating the main characters of the two classical types with those common to both, and comparing them with those found in the case described. In this way it becomes obvious that the case described does not fit accurately into the progressive lenticular degeneration group, nor into that of pseudo-sclerosis. For many of the facts in the following table I am indebted to Hall's painstaking analysis of the published cases, and where figures are mentioned under the heading, "Hepato-Lenticular Degeneration," they are his.

There seems little doubt that practically all the symptoms, and certainly all the motor disabilities found in the diseases comprised under the term "Hepato-Lenticular Degeneration," are due to the diffuse generalized muscular rigidity invariably associated with them. In the case reported, this rigidity was well established and had produced an extreme degree of dysarthria, but it was apparently not so intense as in the classical types of progressive lenticular degeneration; it had not reached the stage where the whole voluntary musculature is permanently rigid during the waking hours; no muscular contractures were present, and a very marked diminution in the rigidity could be obtained if the muscles were put at rest. The patient enjoyed intermissions when at rest, during which the rigidity and its resulting symptoms almost disappeared. In spite of this, the positive nature of the symptoms was certainly of the order found in Wilson's disease, with which is invariably associated a naked-eye destructive lesion of the lenticular nuclei. The pathological examination, however, failed to show any gross change in the brain, and we are forced to look closer into the histological changes found in this case to explain the contradiction.

In pseudo-sclerosis the muscular rigidity and the destructive changes in the lenticular nucleus are minimal; in progressive lenticular degeneration the rigidity is intense and the destruction of the putamina often total. The histological changes in the case described consisted of a pathological neurogliosis which had entirely replaced the normal glial tissue of the putamina and caudate nuclei, and a selective necrosis of the large nerve cells of these nuclei. This change was sufficient to give rise to all the positive signs of Wilson's disease. It appears likely, therefore, that

	All cases grouped together as hepato-lenticular degeneration	Progressive lenticular degeneration	Pseudo-sclerosis	Case reported
Age at onset .. .. Greatest incidence	Between 11 and 25 .. .. Limits : 3 to 41 years ..	Between 15 and 20.. .. Tends to include the younger patients	This type generally in patients in which the onset is between 30 and 45	10 years
Sex	Males predominate : 50 males to 18 females. (Hall)	Sexes appear to be more equally affected	Males predominate	Female
Duration (when disease itself caused death)	2 to 7 years (average) .. Limits— 1 month to 11 years. (Hall)	2 to 7 years (average) .. Limits— 4 months to 7 years (Wilson)	As Wilson's disease	2½ years
Family history ..	Is familial, and in one generation in half the cases. In two cases has appeared in several generations. (Hall)	Equally marked familial tendency	As Wilson's disease	No family history obtained
Motor system— (1) Muscular rigidity	Always present and generalized : degree of rigidity varies ; is not pyramidal ; affects agonists and antagonists equally	Is always a marked feature ; dominates the clinical picture ; may terminate in contracture attitudes	Much less intense ; may escape notice, but often obvious and probably always present	Generalized and intense in movement and standing ; marked relaxation during intermissions ; always very variable
(2) Involuntary movements	Generalized tremor the most common Always increased by voluntary muscular contraction	A salient feature .. .. Increases as disease progresses; the muscular rigidity tends to mask it	Always present, occasionally very marked ; is a striking feature	Always present in voluntary muscular contractions, but not a striking feature otherwise ; of the same type as in preceding
Reflexes..	Not altered .. .. .. Abdominal reflex present ..	Normal, but difficult to elicit when rigidity is intense Abdominal reflexes present	As in Wilson's disease	As in Wilson's disease
Walking	Difficulty in walking present in all cases, but varies within wide limits	Great difficulty always ; progresses to complete inability to walk or stand	Often only moderate difficulty ; rarely so marked as in Wilson's disease	Great difficulty even in standing, walking almost impossible
Facial aspect	Every gradation from facial immobility (of Parkinsonian type) to intense facial spasm	Intense rigidity of facial muscles. Widely-open eyes and mouth. Powerful facial spasms. Tongue muscles rigid	Spasm and rigidity inconspicuous. Immobility and mask-like expression generally	Moderate rigidity only. Mouth not held widely open. Rigidity well marked during attacks of spasm. Face always flushed
General attitude ..	Head and neck may be held rigidly in fixed position	Attitude always one of marked general rigidity	This is generally slight, and	Not very noticeable when at

General attitude ..	Head and neck may be held rigidly in fixed position, and hands in stereotyped positions (e.g., of tetany), with arms adducted; every gradation between this and slight general rigidity	Attitude always one of marked general rigidity	This is generally slight, and may escape notice	Not very noticeable when at rest, but marked and intense under observation. Subject to marked remissions
Speech defect	Varies from slight dysarthria to complete anarthria; always slow and spasmodic; relaxes with the muscular rigidity which causes it	Always present, marked and progressive, reaching complete anarthia. No paralysis or atrophy of muscles concerned	May be a quite slight defect only. Generally present, but to a considerably less degree than in Wilson's disease	Was a striking feature. Speech limited to a few monosyllables
Difficulty in swallowing	Variable, depending on degree of rigidity. Fluids generally easily swallowed	Generally a very marked difficulty	Usually only slight dysphagia	Not a marked feature
Corneal pigmentation	Present in more than half the recorded cases	Has been described in typical cases	Very commonly present ..	Was not specially looked for
Mental state	A varying degree of dementia. Generally slight	Dementia not marked	Tend to show more marked mental change	Not demented. Some diminution of intellectual powers
Abdominal organs ..	Generally no abdominal symptoms. Liver dullness generally diminished	No clinical signs, and only vague symptoms	As in Wilson's disease	Attacks of epistaxis. No other signs
Pathological changes in central nervous system	Nerve-cell destruction and neuroglial proliferation most marked in the corpus striatum but often diffuse, yet of less severe degree, throughout most of the brain. Dentate nucleus and cerebral cortex often involved. Changes vary from gross naked-eye cavitation to discoloration of lenticular nuclei, down to absence of any naked-eye changes	Characterized by naked eye changes, and a sharply demarcated lesion, viz., bilateral, symmetrical softening of the lenticular nucleus, with cavitation of the putamen. This change is present in all clearly cut cases of Wilson's disease. Degeneration of tracts connecting striate body to thalamus, subthalamic body and red nucleus. Economo describes cortico-striate degeneration. A diffuse neurogliosis has been found since Wilson's publication, similar in all respects to that of pseudosclerosis. Occasionally cavitation has been described in the cerebral cortex	No naked-eye changes as a rule, but diffuse degeneration throughout brain. Yet this chiefly in basal ganglia, and especially in lenticular nucleus. The hypothalamus, cortex cerebri and dentate nucleus are often involved. Change is a degeneration and destruction of nerve cells, with marked progressive neurogliosis. Altzheimer describes as occurring frequently in all parts of C.N.S., a neuroglial giant cell. Universal distribution of this cell not confirmed since his description. All observers agree that a diffuse neurogliosis, characterized by large numbers of neuroglial cells with large pale nuclei, is present. This usually found in grey matter only. Hall finds it in the white matter also	No naked-eye changes. Diffuse uniform degeneration of large nerve cells of putamen and caudate nucleus of corpus striatum, with degeneration of its fibre system and marked neurogliosis. Degeneration of fibre system and a prolific vascular new formation in several foci in the cortex, specially in the frontal lobes. Cell degeneration in these foci of cerebral cortex, and in dentate nucleus, but to less degree than in putamen and caudate nucleus. Altzheimer cells not numerous. Wider diffusion of changes throughout the central nervous system not found

	All cases grouped together as hepato-lenticular degeneration	Progressive lenticular degeneration	Pseudo-sclerosis	Case reported
Liver	Gross multilobular cirrhosis with reduction in size of liver always present, and practically always symptomless. Nodules larger than in Laennec's cirrhosis. This probably explained by the youth of the patients (Hall) Histological characters :— (*a*) Very cellular, broad cirrhotic tracts, containing large numbers of proliferating bile ducts. (*b*) Isolated lobules and cirrhotic tracts always very vascular. Vessels are branches of portal vein. (Kleiber and Hall) (*c*) In a few cases foci of necrosis and lobular destruction described	No constant difference noticed in either		disease in this respect Focal necrosis not found

the histological changes described in the lenticular nuclei in the case reported, represent a stage in its functional destruction not far removed from the total degeneration found in well-established cases of Wilson's disease.

As regards the changes found in the other parts of the brain, the small foci of degeneration and vascular new-formation in the cerebral cortex were as striking as they were unexpected. A similar change has been found in the corpus striatum in this disease by Pollock and by Spielmeyer. Pollock found in silver-impregnated preparations of the lenticular nucleus in this disease a dense network of thickened vessels ramifying irregularly and pervading the whole of the putamen. In sections stained by hæmatoxylin and eosin this appearance was not found. Pollock insists that this appearance is only obtained by impregnation methods. Hall found a similar vascular proliferation in the dentate nucleus and red nucleus. He is inclined to regard the change described by Pollack as due to atrophy and retraction of the wasted nucleus. Spielmeyer found a striking proliferation of vessels and of perivascular connective tissue in the most degenerate parts of the corpus striatum. He discovered a similar change in the dentate nucleus, but in neither nucleus any accompanying inflammatory changes. Spielmeyer also found focal lesions in the cerebral cortex of the occipital lobes, in which the changes were of the same type as those found in the lenticular nucleus, i.e., intense nerve-cell degeneration and marked neurogliosis. Howard and Royce have described, in a case having a duration of one month (the most acute case published), cavitation in the caudate nucleus, optic thalamus and red nucleus, similar to that found in the putamen.

It is probable, therefore, that the changes in the cerebral cortex are of the same nature as those found in the lenticular nucleus, but of more recent origin or of a less acute type. I am not inclined to agree with Hall that the vascular new formation is probably due to wasting and retraction of the grey matter. The change described in my case was quite unlike that found in an organ undergoing atrophy, and its intensity was out of all proportion to the amount of wasting. It seems probable that this change is an early stage in the same pathological process which eventually ends in nuclear destruction, and that it appears in extra-lenticular foci, because they are affected later.

It is my pleasant duty, in conclusion, to thank Dr. J. Odery Symes, Physician to the General Hospital, Bristol, for permission to publish the case, for the use of his clinical records and encouragement in the investigation.

I am considerably indebted to Dr. J. V. Blachford, the Superintendent of the Bristol Mental Hospital, for placing at my disposal his intimate knowledge of the anatomy of the nervous system, and for kindly criticism and advice in the preparation of the paper and examination of the material.

Conclusions.

(1) A case is described having all the essential characters of hepato-lenticular degeneration.

(2) It illustrates conclusively, both clinically and pathologically, the existence of transition types between Wilson's disease and pseudo-sclerosis.

(3) Focal lesions in the cerebral cortex, characterized by a prolific vascular new formation, are described.

(4) A selective necrobiosis of the large motor cells of the putamina and caudate nuclei was found histologically.

(5) It appears probable that:—

(*a*) An early stage in the destruction of nervous tissue in these diseases is the development of a specific type of vascular new formation.

(*b*) The changes described in the lenticular nuclei in the case reported represent a late stage in their degeneration.

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RHYTHMICAL CONVERGENCE SPASM OF THE EYES IN A CASE OF TUMOUR OF THE PINEAL GLAND.

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THE study of the symptomatology of tumours of the pineal gland has brought to light a great many facts, but there is still much to be learned. It is, therefore, necessary that all cases that may contribute to a fuller knowledge of this subject be described, and for this reason I record here a case with remarkable clinical symptoms:—

H. K., aged 14, came of a neuropathic family. A sister of the father's was epileptic; the paternal grandfather indulged in alcohol to excess, and the mother and maternal grandmother were abnormal. A brother of the father suffered from tuberculosis. The parents are healthy and have had two children only; there were no miscarriages. The patient's brother is healthy. The patient's birth was attended with difficulty, instruments being used, but, as far as can be ascertained, no permanent bad consequences ensued. The child's development was normal; he learned to walk and speak at the normal time, and he was clean in his habits at an early age. He did not suffer from nocturnal enuresis. He has had no serious illness and was not subject to fits. He was a gentle, somewhat nervous boy, who did not get on very well at school, partly because he was playful and inattentive.

In December, 1919, he began to look ill, became thin, and complained of a singing noise in his left ear, headaches and dizziness; he often stayed in bed for the day. In January, 1920, there came a sudden change for the worse; his temperature rose to 40° C. and he had violent headaches and loud singing in his ears. The fever gradually diminished, but he remained ill and began to squint. He exhibited a pronounced tendency to undue sleepiness; sometimes he slept all through the day. Gradually the illness took the form it presented in September, 1920, when he came under observation.

He was a rather broad-shouldered but short boy, the shortest but two in his class at school, though he was one of the oldest. He had a flabby appearance with deposition of fat chiefly round the breasts and the abdomen; this was the more striking as he was much thinner than he had been formerly. Since March his weight had increased by 7·5 kilog. There was no swelling of the glands, the pulse-rate was 80 and always regular, respiration was quiet but his temperature now and then rose a little above the normal. Smell was

not affected. Vision was $\frac{3}{4}$ in both eyes, which were emmetropic. The visual fields were concentrically limited in a small degree and in both eyes there was a papillitis, with a swelling of $3\frac{1}{2}$ D. in the right eye and 4 D. in the left. The pupils were equal, of medium size and regular in outline; there was no hippus. The reaction to light was exceedingly slight in the right eye, totally absent in the left; on the other hand the reactions on convergence and to pain could be easily elicited. There was convergent strabismus, which increased and decreased suddenly at intervals, so that a rhythmical spasm of convergence ensued. The converging phase of this movement was rapid, the diverging phase slower. The right eye moved fully into the outer canthus, the left eye not quite so much, but the difference was small. There was almost complete conjugate paralysis of upward and downward movements. Adduction and rotation were undisturbed. He did not complain spontaneously of seeing double, but with the red-green spectacles diplopia appeared to exist, the images being homonymous and their mutual position changing little with change in the direction of gaze. Now one image, now the other was slightly oblique. The double images separated further when the object that was to be focused was moved to a greater distance for him. Sensibility in the area of the trigeminal nerve was undisturbed, and the corneal reflexes were present on both sides. The right masseter and temporal muscles contracted less vigorously than those on the left side. The jaw reflex was diminished, and the floor of the mouth was possibly somewhat softer on the left than on the right side. The left side of the face seemed slightly paretic but the facial muscles reacted normally to electric stimulation. There was some diminution of hearing on the left side with shortened bone conduction, while Weber's test showed some lateralization towards the right; this may have been due to slight sclerosis of right tympanum. Rinne's test gave a normal result on both sides. Taste was unaffected. The left side of the pharyngeal arch was somewhat broader than the right, but both moved equally well. Phonation was normal but speech was impeded, slow and scanning. The sternomastoid and the trapezii muscles contracted well. The tongue protruded straight and there was no lingual tremor. There was nothing particular to be observed in the teeth and palate; the pharyngeal reflex was present. The thyroid gland was not enlarged.

It is remarkable that the patient never kept his head still; it was continually in a slight irregular motion. There were no disturbances of sensibility on the neck or chest. No abnormalities in the heart or lungs, or enlargement of the thymus could be detected. The movements at the neck and the spine were free. There was no pronounced dermography or hyperæsthesia. There were incessantly small irregular movements of both arms while they were at rest, and involuntary movements, producing a form of intention tremor or atasia, in movement which gave a certain clumsiness to more delicate actions, as tying knots or writing. Muscular power was poor, slightly less in the left than in the right arm (the boy was right-handed). Muscular tone was normal. There was slight dysdiadochokinesia in the left arm, but no deviation in the pointing

tests. The tendon and periosteal reflexes were diminished, and equally so on both sides. The sense of touch, pain, cold, heat, and the sense of position and stereognosis were not impaired. The abdominal organs presented nothing worthy of mention. The right lower abdominal reflex was diminished. Sensation on the skin of the abdomen and loins was not impaired. Both the penis and the testicles were remarkably small, and the growth of pubic hair was scanty. The cremasteric reflex was present. The legs, as the arms, were never still. The strength of both was good, there was no ataxy and the tone of their muscles was normal. The knee-jerks were brisk and equal but there was no clonus. The reflexes of Babinski, Oppenheim and Rossolimo could not be elicited. Sensation was undisturbed in the lower limbs. He could bend the body backwards and raise it again to the sitting position with crossed arms. Romberg's phenomenon was absent. He walked and stood unsteadily.

The urine contained no albumen, and no sugar even after taking 100 gr. of glucose on an empty stomach. The reactions of Wassermann and Sachs-Georgi (Bok's quantitative method) gave repeatedly negative results in the serum and cerebrospinal fluid, as well as in the blood of both parents. Nonne's reaction was sometimes faintly positive; Pandy's reaction was often so. The cerebrospinal fluid contained 40 cells per c.mm.; these were lymphocytes and plasma cells. Micro-organisms were never found and guinea-pigs injected with it did not develop tuberculosis. Its pressure was on an average 50 cm. of water. These values were pretty regularly found in the frequent lumbar punctures which were made for therapeutic purposes. Von Pirquet's reaction was weakly positive. The cell count in the blood was about normal. No abnormalities were detected in radiographs of the cranium and the sella turcica was not enlarged. Examination of the labyrinthine reflexes by Bárány's methods elicited strong reactions and the patient soon began to vomit. This, added to the rhythmical convergence spasm of his eyes, rendered examination exceedingly difficult and unreliable.

He exhibited no defects of intellect, though he was emotional in a high degree and cried readily. He did not suffer much from headaches and seldom vomited.

In coming to a clinical diagnosis we were influenced by the following considerations: There must exist a localized process in the skull, the nature of which it was not possible to determine with certainty. Lues could be excluded with probability, but we could not decide between an inflammatory process or a tumour. The neurological symptoms suggested that the disease involved the corpora quadrigemina. The following considerations led to this conclusion: there was a typical conjugated paralysis of upward and downward movement of the eyes; Argyll-Robertson's symptom which has been found in quadrigeminal tumours (Kinnier Wilson [47], Bruns [10], Rorschach [39] and others);

light auditory disturbances; the general motor and static unrest might be regarded as a mild form of the choreic and athetotic movements which occur in quadrigeminal affections. The disturbances of equilibrium in standing and walking, and the affection of co-ordination of the more delicate movements, reminded us of the combination of intention tremor, ataxy and athetosis described by v. Oordt [36]. The somnolence, which had been present in the beginning of the illness, and the disturbances of speech also pointed in the same direction. There were, however, indications that the disease had already extended caudalwards and ventralwards; the slight paresis of the face and the involvement of the root of the trigeminal nerve might be attributed to this. After the operative decompression which was performed later, the paresis of the jaw disappeared, hence I assumed that the lesion of the trigeminal nerve was due to increased cerebral pressure and compression of the ganglion Gasseri and the third branch of the nerve against the petrous bone, as in the case described by C. F. van Valkenburg [45]. In addition to these neurological signs there was a tendency to adiposity and an exceedingly small development of the penis and the testicles, that is a type of a dystrophia adiposo-genitalis which was regarded as secondary to distention of the third ventricle. Jelliffe and White [28] described the occurrence of dystrophia adiposo-genitalis in cases of hydrocephalus internus with closure of the aquæductus Sylvii. Consequently the clinical diagnosis was a morbid process which destroyed the corpora quadrigemina.

It was possible to confirm the diagnosis after death, though the brain was removed under very difficult circumstances. An account of the autopsy follows.

After the dura mater and the falx had been removed from between the hemispheres a tumour of the size of an almond was found at the place where the falx and the two halves of the tentorium cerebelli join. This tumour had a short stem on its anterior side which was torn through. No disease could be detected in the soft meninges. The cerebral gyri were broad and flattened, and the sulci were narrow. There was a hydrocephalus internus with pronounced widening of the lateral and the third ventricles. In the situation of the epiphysis and the corpora quadrigemina a tumour mass was found of the size of a nut, which extended dorsally and bent round the splenium of the corpus callosum, presenting there a severed stem, which evidently was connected with the stem of the tumour removed with the dura. The

upper pole of the cerebellum was flattened by the tumour, and the thalami had been pressed aside. The tumour in the hard meninges was fairly firm, sharply separated from its surroundings and of a regular form; that in the position of the epiphysis on the other hand was loose, soft, friable and irregular in shape. It was connected with the tela choroidea. Though the two tumours did not resemble each other macroscopically, and if they had not been clearly connected by a stem one would have been inclined to assume two mutually independent growths, yet under the microscope all parts of the growth appeared to belong to the type of epiphysis tissue which is found in young individuals. In the first place it contained cellular tissue septa, which in

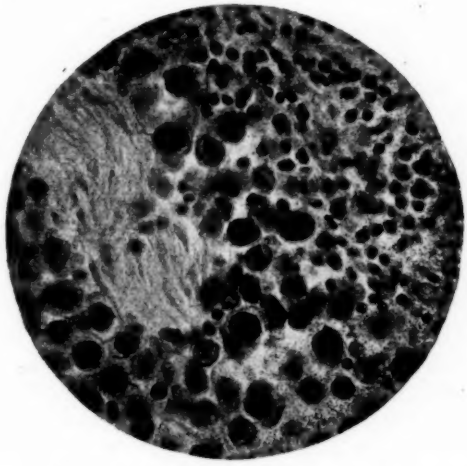

FIG. 1.—Photomicrograph of the tumour.

the main mass were loose-meshed, and in the dural growth were thin and compact. Between the septa lay irregular groups of polygonal large cells with large pale nuclei, and between them groups of small cells, poor in protoplasm and possessing dark round nuclei. These latter cells resembled lymphocytes. The microscopical picture agreed entirely with that of the outer layer of the teratoma of the epiphysis described by Hymans van den Berg and van Hasselt [27], preparations of which I have been able personally to examine through Dr. van Hasselt's kindness. The rest of the tumour corresponded with the description and illustration which Löwenthal [30] gives of an epiphysis tumour examined by him. Löwenthal regarded his tumour as an "adenoma

maligna." Though macroscopically the resemblance to Löwenthal's specimen was very great, the connecting stem with the falx cerebri was absent in his case. I have succeeded in finding this in one case only in the literature, i.e., in v. Frankl Hochwart's remarkable teratoma [18]. The place of attachment was there the same as in our case, viz., the point where tentorium cerebelli and falx cerebri meet. In v. Frankl Hochwart's case there was, however, no tumour tissue between the layers of the dura mater.

In consequence of the difficult circumstances attending the autopsy a complete examination could, unfortunately, not be performed, and the other organs of internal secretion could not be investigated. The hypophysis was not examined.

This case of epiphysis tumour presented many points of interest; it may be compared with other cases recorded in literature.

In the first place the movements of the eyeballs must be discussed at more length. There was a fairly regular rhythmical convergence, consisting in a rapid phase of convergence and a slow phase of divergence. Professor Dr. W. P. C. Zeeman, who examined the patient, was so kind as to allow me to see his notes. He described the phenomenon as "continual abrupt converging of the eyes." The deviations resembled those of a nystagmus of medium degree. The frequency of the oscillations was smaller than those of the nystagmus, about one or two occurring every second. They were not regular in rate, and were best observed when the patient looked straight in front of him without accurate fixation; on intentional focusing the movements continued but were less easy to see.

How should these phenomena, which, as far as I know, have never yet been described, be interpreted? They were undoubtedly related to the existing convergent strabismus which presented some peculiar characteristics, for the double images hardly changed their relative positions when the patient looked to the right or the left, but they moved farther apart when the object to be focused was moved farther away.

Hence there was here either spasm of convergence or paresis of divergence. It is the more difficult to decide which of the two was present, as ophthalmologists are not agreed on the existence of the latter. Straub [43] states that a paresis of divergence may occur; Bielchowski [8], on the other hand, is of opinion that one is never justified in assuming the existence of divergence paresis. It may, however, be pointed out that the spasm of convergence, if it existed,

was not accompanied by disturbances of accommodation or change in the pupils. On the whole little is found in textbooks of neurology on spasm of the ocular muscles. Hysteria is regarded as the most common cause of spasm of convergence, but it occurs also in meningitis. Ophthalmologists devote more attention to it, and others too lay stress on its hysterical ætiology. Straub mentions cerebral tumours and abscesses as causes of paralysis of divergence. Körber's nystagmus retractorius may be mentioned as another form of rhythmical movement of the eyeballs, which cannot be classed with the more generally known forms of nystagmus, and which possibly presents some relationship to the movements in my case. This phenomenon consists in the eyeballs being rhythmically drawn backwards. Bárány [4] describes the phenomenon as present in one eye in a case of a tumour of the corpora quadrigemina. The retraction was synchronous with the nystagmus of the other eye. Elschnig [14] found nystagmus retractorius twice with affections of the aqueduct of Sylvius; in these cases the convergence increased somewhat with the rhythmical retraction of the eyeballs.

Another peculiarity in the eyes was the existence of Argyll-Robertson's sign. Dejerine [13] states in his well known textbook that the Argyll-Robertson phenomenon combined with lymphocytosis of the cerebrospinal fluid is pathognomonic of syphilis. This rule appears, however, not to hold good in this case, and accordingly not to be of universal validity.

Another point of interest is the nature of the trophic disturbances. These were certainly not typical of an epiphyseal tumour; the genitals were small rather than large, the growth of genital hair was not excessive, nor was the amount of hair on the body exceptional. He was also rather small for his years, and there was no extraordinary precocity in his mental development. Why did the syndrome of macrogenitosomia præcox, so typical of epiphyseal tumours, not exist in our case? As early as in 1909 Marburg [32] surmised that the pineal gland has an internal secretory function, which normally inhibits the development of the genital organs. This standpoint has been made more plausible by subsequent clinical observations, and the animal experiments by Foa [19] point in the same direction. He found after the removal of the epiphysis in cocks a hypertrophy of the secondary sexual characters. Similar experiments were performed in mammals by Sarteschi [40] with the same result. Other investigators, however, as Dandy [12] and Exner and Boese [15], could not confirm Sarteschi's results.

Askanasy's theory [1] is opposed to the hypothesis that a distur-

bance of internal secretion is the cause of the trophic disturbances. He takes the view that the trophic disturbances are dependent on the tumour itself. He is of opinion that all epiphyseal tumours accompanied by hypergenitalism which have been examined, consisted of embryonic tissue; the cases of Ostreich-Slawyk [37], Holzhäuer [25], Goldzieher [23] and Ogle [35], were not sarcomata as the authors erroneously assumed, but teratomata or allied chorioepitheliomata. It is only for Raymond and Claude's case of glioma [38] that Askanazy cannot account. He rests his theory on the fact that teratomata in other parts of the body have occasionally caused hypergenitalism. He considers the existence of a teratoma as a kind of "gestation," which may give rise to a peculiar development in a boy. All things considered Askanasy's view does not seem very plausible, and the fact that there was no teratoma or epithelioma present in our case does not explain why the syndrome of macrogenitosmia præcox was not present. I would rather attribute the cause to our patient's age, for though it is certainly not true that trophic disturbances do not appear after the seventh year as Marburg assumed, there is an age limit which seems to lie about the twelfth year; only Goldzieher's case [23] is an exception.

The following table records the ages of the cases of epiphyseal tumour with macrogenitosomia præcox, which were anatomically confirmed.

Goldzieher [23]	16 years,	angioblast sarcoma
Bailey and Jelliffe [3]	12 ,,	teratoma
Raymond et Claude [38]	10 ,,	glioma
Takeya [44]	10 ,,	teratoma
Odermatt [34]	10 ,,	teratoma
Boehm [9]	9 ,,	teratoma
Hymans v. d. Berg en v. Hasselt [27]	8 ,,	teratoma
Gutzeit [24]	5 ,,	teratoma
Steiner und Johan [42]	7 ,,	adenoma
Ogle [35]	6 ,,	alveolar sarcoma
v. Fränkl-Hochwart [18]	5 ,,	teratoma
Holzhäuer [25]	4 ,,	sarcoma
Ostreich-Slawyk [37]	4 ,,	psammo-sarcoma

When we contrast with these cases those of teratoma in which macrogenitosomia did not occur, we see that the age was then always 12 years or more.

Gauderer [21]	12 years
Coats [11]	13 ,,
Weigert [46]	14 ,,
Falkson [16]	16 ,,
Hueter [26]	19 ,,
Fukuo [20]	19 ,,
Schmincke [41]	22 ,,
Neumann [33]	27 ,,

It follows from these facts that macrogenitosomia cannot be expected to develop in a boy of 13 years. Nevertheless all symptoms of disturbance of internal secretion were not absent, for there were unmistakable indications of dystrophia adiposo-genitalis. This syndrome occurs sometimes with epiphyseal tumours (Jelliffe and White) [28]. But the question has not been satisfactorily decided yet in how far the disturbance of the epiphyseal function can cause adiposity. It is certainly not constantly associated with typical macrogenitosomia præcox. Falta [17], Cushing and others, consider adiposity to be a hypophyseal phenomenon which has nothing to do with an internal secretion of the epiphysis. In our case, where a complete hypophyseal picture existed, this view seems very probable, since the hypophysis would be hampered in its function by the dilatation of the third ventricle which compressed the infundibular region. This interpretation seems the more plausible, since Frölich's syndrome is also found in cases of tuberculosis of the floor of the third ventricle, and in a case of injured infundibulum with intact hypophysis Lereboullet, Mouzon and Cathala [29] found the condition of dystrophia adiposo-genitalis. It is still, however, remarkable that as a rule no adiposity co-exists with ordinary hydrocephalus, though cases are known in which it did occur (Goldstein [22]). It may be that the pressure relations due to a tumour of the mesencephalon producing closure of the aqueduct of Sylvius and pressure on the blood-vessels of the choroid plexus, is different from those of an ordinary hydrocephalus. These views are in conflict with Marburg's hypothesis, which attributes the adiposity to hyperpinealism. Marburg's theory, however, does not seem probable since it is hardly possible to assign a specific hyperfunction to the glioma that existed in Raymond and Claude's case.

Summarizing the special features which this adenoma of the epiphysis presented, we see :—

(1) There was rhythmical spasm of convergence.

(2) There was Argyll-Robertson's sign with lymphocytosis of the cerebrospinal fluid, not due to cerebrospinal syphilis.

(3) The disturbances of internal secretion were the same as those found with dystrophia adiposo-genitalis.

(4) The tumour consisted of two parts connected by means of connective tissue, one part lying in the situation of the epiphysis, the other part between the folds of the dura mater where the falx cerebri and the tentorium cerebelli meet.

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THE INFLUENCE OF THE CEREBRUM AND CEREBELLUM ON EXTENSOR RIGIDITY.

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INTRODUCTION.

THE condition of decerebrate rigidity which manifests itself as a prolonged and enduring contraction of the extensor muscles, especially those which oppose the action of gravity when the animal is standing, was shown by Sherrington [7] to result from decerebration at the level of the mid-brain. It is readily produced experimentally in the higher mammals, cat, monkey, &c., by the ablation of the cerebral hemispheres. Sherrington found that if he removed only one hemisphere the rigidity appeared to be rather inconstant in its production and non-persistent, but was perhaps more marked on the ipsilateral side. He further showed [8] that decerebrate rigidity is abolished when the continuity of the proprioceptive reflex arcs is interrupted. The afferent path of these reflex impulses ascend to the brain by way of Gowers', or the ventral spino-cerebellar tract, and not by the dorsal columns, since the rigidity is unaffected by cutting the latter. The efferent impulses do not pass by way of the pyramidal tracts, but appear to descend in the cord by some tract originating in the region of the red nucleus. Sherrington [10] considered that the cerebellum was not an essential link in the production of decerebrate rigidity, since this condition often remained after the removal of the cerebellum.

Thiele [11] attempted a further analysis with the idea of discovering the tracts, centres and place of origin in the brain of the impulses leading to decerebrate rigidity. He came to the conclusion that this condition is not due to the removal of the cortical influence, but of a thalamic one; and furthermore, that this thalamic influence is transmitted along a tract which decussates high up in the mesencephalon. The result of cutting this tract far forwards, therefore, is rigidity on the opposite side of the body, while a section posterior to the anterior corpora quadrigemina gives ipsilateral rigidity accompanied by slight contra-

lateral rigidity. Thiele found that the cerebellum exerted an influence on decerebrate rigidity, since extensor rigidity appeared after each of the following operations: removal of the tentorium, division of the vermis, unilateral ablation of the cerebellar cortex. Rigidity could be abolished by destroying the dentate nucleus or by cutting the trapezal fibres in the pons. The results of his experiments led him to express the view that there are two antagonistic forces acting on the ventral horn cells of the cord; one from the thalamus exercising an inhibitory influence upon the contralateral side, the other from Deiters' nucleus exercising an augmenting influence; an indirect control may be maintained by the cerebellar cortex, since it exerts an inhibitory influence on Deiters' nucleus.

Weed [12] concluded from his experiments that the main centre and the source of decerebrate rigidity lay in the red nucleus in the mid-brain. The work of Magnus [3] and Bazett and Penfield [1], however, has proved that the red nucleus is not the centre for decerebrate rigidity, since rigidity persists after transection of the brain-stem posterior to this nucleus. Bazett and Penfield locate the centre for decerebrate rigidity at the level of Deiters' nucleus.

According to Weed there are two inhibitory influences acting on the dentate nucleus, one from the cerebellar cortex, as Thiele, and more recently Miller and Banting [5], have shown, the other from the cerebrum. The course of this latter tract was shown definitely to lie in the mesial anterior fraction of the internal capsule above the thalamus, and in the mesial fraction of the crura cerebri. Thus the inhibitory pathway cannot originate in the thalamus as Thiele had supposed, but it apparently arises from the cerebral cortex. Weed demonstrated that it runs caudad in the mesial part of the internal capsule, and inferred that its fibres ended in the pontile nuclei. The tract passes eventually to the cortex of the cerebellum by way of the contralateral middle cerebellar peduncle. Sherrington [9] had suggested such a tract earlier.

The apparently contradictory results—namely, that in one case ipsilateral and in the other contralateral rigidity was produced by unilateral cerebral ablation—Thiele explained by the difference in level of the section, ipsilateral rigidity resulting if it were at a high level and contralateral rigidity if at a low level. Weed, on the contrary, found that ipsilateral rigidity resulted no matter at what level the section was made.

Our object in this investigation was the discovery, if possible, of the

exact location of the inhibitory pathway, and the effects produced by its destruction at various levels.

Experimental Results.

(1) *Technique.*—All our experiments were performed on cats, and no experiments reported here were survival experiments, i.e., the results were obtained within twenty-four hours after the first operation.

The animals were deeply anæsthetized and a tracheal cannula inserted, after which anæsthesia could be continued, or artificial respiration given. In the first few experiments the carotid arteries were tied previous to any operation on the skull. This practice was soon discontinued because it was found that in certain animals the mere interference in this manner with the blood supply to the brain produced a marked degree of extensor spasm.

In disclosing the brain an ordinary trephine, $\frac{3}{4}$ in. in diameter, was used. Hæmorrhage was controlled by the application of wax to the cut edges of the bone, and of hot saline packs over the whole area of operation. No serious hæmorrhage was encountered in a series of forty animals, so that any lack of extensor rigidity was never caused by an enfeebled condition consequent upon the loss of blood. The brain could be kept in an excitable condition only by the continued application of warm saline sponges. This procedure was found to be most important, for unless the circulation in the choroid plexus remained good, the cerebral cortex quickly became inexcitable (cf. Miller and Banting).

There are several other factors besides the tying of the carotids which have an effect on extensor muscle tone. Chief among these is the position in which the animal is lying, especially the relation of the head and neck to the rest of the body (Magnus and Kleijn [4], also Bazett and Penfield, p. 197). If the animal is lying on its side with its head raised, the limbs on the side of the body in contact with the table normally exhibit a greater degree of rigidity than those on the other side. This effect can be readily demonstrated by testing the rigidity of the front or hind limbs of a decerebrate cat lying on its left side. The left fore and hind limbs will exhibit greater extensor rigidity than the right ones. But upon turning the animal over on its right side the right limbs become at once the more rigid. Therefore when a test of the degree of rigidity was being made in an experiment the animal was

suspended on its abdomen in a trough and the position of the limbs noted as they hung freely in the air, or still better a comparison was made of the force necessary to bend the right and left legs at the knee or elbow when the animal was suspended in the trough or lying flat on its back. In the latter case a spring balance was sometimes used to register the number of pounds of pressure necessary to cause bending of the limb. This varied from a few ounces to 3¼ lb., depending on the state of extensor tone. Ether anæsthesia also profoundly affects muscle tone. If the animal is lightly etherized it shows marked extensor rigidity very similar to, if not identical with, decerebrate rigidity. Ether rigidity, however, is always bilateral and is fairly transient, probably due to inability to maintain a constant degree of anæsthesia; also it is often interrupted by clonic movements. Sometimes ether rigidity was purposely induced for experimental reasons, but when such a condition might obscure rigidities of other origin, the animal was allowed to come completely out of anæsthesia before the rigidity was tested, or the anæsthesia was deepened until the ether effect had disappeared, but rigidity due to nervous lesions persisted.

In cutting parts of the cerebrum, the cerebellum, or their peduncles, a very sharp scalpel was used, but if the incision had to go far into the cranium and there was danger of injury to the venous sinuses, a blunt instrument was employed.

For cortical or nerve tract stimulation a unipolar stigmatic electrode was used. A large zinc plate applied to the back of the animal and covered with gauze moistened with saline served as the other pole. The source of stimulation was an interrupted current from an inductorium. The strength of the current was not measured, but it was just strong enough to cause contraction of the scalp or jaw muscles when applied directly to them. When the cortex or cut surface of the brain was dry the effect of the stimulus could be noted almost immediately, but if there was hæmorrhage five to fifteen seconds often elapsed before stimulation became effective. No currents strong enough to spread to the jaw, scalp or neck muscles were used.

(2) *Influence of cerebrum.*—These experiments were undertaken with the object of ascertaining the effect of high and low section of one cerebral hemisphere, and of tracing to the cortex, if possible, the inhibitory tract found by Weed in the mesial part of the internal capsule. The first experiments to be described are those which resulted in the production of extensor rigidity.

In some fifteen cats marked contralateral extensor rigidity of fore

and hind legs followed the ablation of the whole of one cerebral cortex anterior to the optic thalamus. (The results obtained are similar to those described in Cat 53.) The rigidity was quite persistent both during anæsthesia and also when the animal was fully out, except during the mimetic walking movements which always occur at frequent intervals after this operation. The thalamus in these cats was still intact, and although mimetic movements may possibly originate from lower segments, they never persist unless the thalamus remains. The ipsilateral side often showed some slight increase in extensor tone, but this was inconstant and not marked. No rigidity of the neck or tail was noted under these conditions.

Further section caudad by successive slices through the thalamus did not increase the rigidity, but in one cat section of one cerebral hemisphere just below the level of the anterior corpora quadrigemina produced ipsilateral rigidity with very slight increase in tone on the contralateral side. The rigidity thus produced was similar in character to that produced by high cerebral ablation, in that it was not as constant or marked as the rigidity produced by removal of both cerebral hemispheres, but differed in that it was chiefly ipsilateral. This bears out Thiele's statement that the question whether ipsi- or contralateral rigidity shall result after removal of one cerebral hemisphere depends upon the level at which the cut is made.

Cat 58.—9.30 a.m. anæsthetized. Trephined over left occipital lobe. Cut down through left cerebral hemisphere just posterior to anterior corpora quadrigemina to base of the skull. Did not remove this part of brain, but left it inside skull. Ether discontinued.

10.15 a.m.: Cat raises head. Rigidity on both sides, but much more marked on left side in both front and hind limbs.

10.20: Claws with left front leg violently. Left front leg then becomes very rigid. Both front legs now become flaccid.

10.24: Rigidity returned in all four legs. Left legs more rigid than right. Cat raises itself off the table.

10.40: Suspended in trough. Left legs more rigid than right, and more difficult to pull out when forced into position of flexion, i.e., some spasticity on left side.

10.45: Ether given again.

The motor area in the cerebral cortex in several cats was mapped out by unipolar stimulation, and it was found to correspond very exactly with the area described by Campbell [2], i.e., the region surrounding the sulcus cruciatus (fig. 1). Definite flexor and rarely extensor movements of the contralateral limbs could be elicited. Stimulation of the cortex

just ventral to the sulcus elicited flexion of the opposite fore leg. Slightly more lateral stimulation elicited flexion of toes of opposite fore leg; still more lateral elicited flexion of opposite hind leg; stimulation above the sulcus gave extension of the opposite fore leg. When the motor area was cut away to a depth of 5 mm. below the surface on one side, there was no increase in extensor tone on either side of the body. If, however, the frontal area which lies ventral and slightly medial to the motor area was also removed, definite rigidity developed at once in the contralateral fore and hind legs.

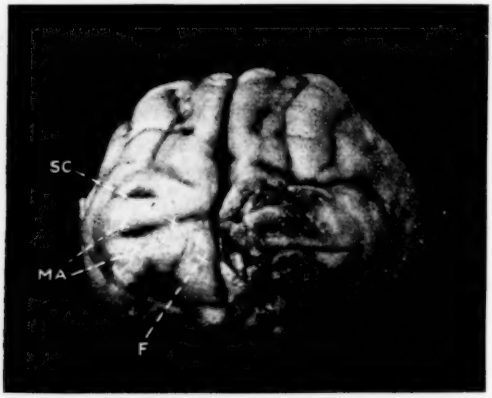

FIG. 1.—Photograph of brain of cat No. 56. S.C., Sulcus cruciatus; F, Frontal lobe; M.A., Motor area.

Cat 55.—Anæsthetized. Trephined over left motor area; tested surface of motor area, and it gave flexion of right leg. Part of left motor area now removed. Cat out of ether and no rigidity in either front or hind legs. Etherized and made a second cut to mid-line on left side, removing all of motor area. Cat out of ether. No rigidity developed. Frontal area found to be still intact. Anæsthetized, and a third deep slice made on left side. Decerebrate rigidity at once on right side. Frontal area found to be removed. Stimulated cut surface of motor area, flexion of right hind leg.

If the frontal area alone was removed, contralateral rigidity resulted, even though the motor area, as shown by stimulation, was still intact. The rigidity resulting from removal of frontal areas may be masked by the voluntary movements which are possible because of the presence of the motor area; deep anæsthesia does away with these movements and leaves the extensor rigidity evident.

Cat 53.—10.20: Anæsthetized deeply. Trephined on left side. No rigidity as result of trephining.

10.35: Stimulated cortex near sulcus cruciatus, contralateral fore foot flexed.

10.37: Cut through anterior part of left frontal lobe. Rigidity at once in right fore limb and to a less degree in right hind limb.

10.50: Motor cortex responds to stimulation; also mimetic movements with all four feet occurred, because animal is coming out of ether.

10.51: Both fore legs now rigid, ether rigidity. Stimulated cut surface of left frontal lobe, right fore leg immediately goes limp, not flexed. Left leg unchanged in rigidity, motor cortex still excitable. Nearly a minute necessary to restore rigidity in right leg. Ether discontinued. Cat out of ether. All four legs move actively.

11.9: Etherized until ether rigidity developed again. Stimulated cut surface of left frontal lobe. At once rigidity disappears from right fore leg.

11.10: Motor cortex excitable. Ether discontinued.

11.12: No rigidity when out of ether. All four legs capable of voluntary movement. Observations repeated in the next few minutes.

Extensor rigidity therefore appears after operations on the cerebral cortex only if the frontal area has been injured.

The results of our experiments on modifying the degree of rigidity, once it has been produced, are as follows: If extensor regidity had been produced by removing both cerebral hemispheres just posterior to the anterior corpora quadrigemina, stimulation of the cut brain-stem on the one side produced an immediate cessation of rigidity on the *ipsilateral* side. But if rigidity had been produced by removing both cerebral hemispheres anterior to the anterior corpora quadrigemina, stimulation of one cerebral peduncle was found to give two distinct effects. If the stimulating electrode was placed on the lateral side of the peduncle, movements of the contralateral limbs were produced, i.e., the pyramidal tracts were evidently stimulated. These movements consisted in vigorous flexions, or sometimes rhythmic extension and flexion. If, however, the electrode was placed on the mesial side of the peduncle no movements occurred, but on the *contralateral* side the extensor rigidity immediately disappeared. At first it was thought that this disappearance of extensor rigidity resulted as an act of flexion, but this was not the case, as this limb merely went limp, and all the muscles became flaccid. The limpness remained for 5 to 10 seconds after removal of the stimulus before the muscles regained their former extensor tone.

When one cerebral hemisphere had been cut away above the thalamus and contralateral rigidity was therefore present, stimulation of the outer part of the internal capsule elicited movements of flexion and extension in

both fore and hind limbs on the contralateral side. If, however, the mesial part of the anterior limb of the internal capsule was stimulated, the *contralateral* fore and hind limbs became limp, returning to their former state of rigidity shortly after the stimulus was removed. Similarly if the motor and frontal areas of the cerebral cortex on one side were removed, points were found on the more posterior parts of the cut surface which gave contralateral movements, and on the more anterior and mesial parts, a point which invariably gave inhibition of contralateral rigidity. And finally, if the frontal area alone was removed, the motor area being left intact as proven by stimulation, the rigidity on the contralateral side immediately disappeared upon stimulation of the cut surface (see Cat 53). Although the motor and frontal areas are close together there was no spread of current, since the effects of stimulating the two areas were strikingly different, in one case active, forceful flexion or strong rhythmic movements, and in the other passive flaccidity.

The extensor rigidity caused by light ether anæsthesia was used to demonstrate the inhibitory function of the cortex of the frontal lobe. Here also it was found that the rigidity in the contralateral side immediately disappeared upon stimulation of one frontal cortex (see Cat 53).

(3) *The influence of the cerebellum.*—In the course of our experiments we investigated the relation of the frontal inhibitory tract to the cerebellum, and we were able to confirm the following observations made by other investigators. (1) Injury to the cellebellar cortex causes ipsilateral rigidity (Sherrington, &c.); (2) removal of the tentorium on one side produces ipsilateral rigidity (Thiele), probably through injury to the cerebellar cortex; (3) if extensor rigidity is present, removal of one half of the cerebellum, or injury to one dentate nucleus, causes rigidity to disappear from the ipsilateral side (Weed); (4) stimulation of the anterior surface of vermis gives an immediate and general relaxation of rigidity (Sherrington, Miller and Banting, &c.). We also found that if successive sections were made through the mesencephalon in a caudad direction extensor rigidity suddenly disappeared when the region of the posterior corpora quadrigemina was reached. Histological sections taken from the various levels showed that rigidity had disappeared when the cut passed through the pontine nuclei posterior to the red nuclei.

Although the cerebellum does not appear to be absolutely essential for production and maintenance of decerebrate rigidity, since Magnus

[3] and others have confirmed Sherrington's observation that the decerebrate rigidity may appear after total removal of the cerebellum, yet the influence of this organ on decerebrate rigidity is most pronounced, as shown by the results given in the preceding paragraph. It seemed probable, therefore, that the inhibitory path from the frontal lobe might be connected with the cerebellum. The relationship is shown in the following experiments: Rigidity was produced on one side, e.g., the right, by removal of the left cerebral cortex above the thalamus. The cerebellum was exposed without injury to the tentorium and enough of the skull removed to make the right middle cerebellar peduncle accessible. The inhibitory tract was then stimulated and the rigidity in the right fore limb at once disappeared. This was repeated several times, so that there was no doubt that the stimulating electrode was applied to the proper place. The position of the electrode was kept unaltered and the right middle cerebellar peduncle was quickly severed. The inhibitory tract was at once stimulated as before, but there was no effect on the rigidity. This experiment was repeated on another cat with the same result. The inhibitory tract was interrupted by cutting the middle cerebellar peduncle on the side showing decerebrate rigidity. Section of the peduncle on the opposite side did not interfere with the action of the inhibitory tract.

Further proof that the inhibitory tract passes through the middle cerebellar peduncle is shown in the following experiment. The cerebellum was carefully exposed in an etherized cat and the middle cerebellar peduncle alone was cut. The animal at once showed ipsilateral rigidity exactly similar to that produced by unilateral cerebral ablation. Deep anæsthesia was necessary since the cat's voluntary movements when it came out of ether made impossible the detection of increased extensor tone. We did not experiment with the superior and inferior cerebellar peduncles since Weed had already shown that the tracts which run through them do not contain fibres which upon stimulation inhibit decerebrate rigidity.

Summary of Experimental Results.

(1) *Production of decerebrate rigidity.*—Ablation of the motor cortex of the cerebral hemispheres did not result in the condition of extensor rigidity. Rigidity occurred only if the frontal areas were destroyed. If one frontal area was removed, or the cerebral hemisphere cut so that the fibres arising from the frontal lobe and running in the internal capsule were interrupted anywhere in their course down to

about the level of the anterior corpora quadrigemina, contralateral rigidity resulted with slight ipsilateral rigidity. Successive sections through the entire hemisphere did not appear to increase the degree of rigidity resulting after destruction of the frontal area, but the rigidity disappeared when the section passed through the posterior corpora quadrigemina. Hemisection of the brain-stem posterior to the anterior corpora quadrigemina produced mainly ipsilateral rigidity, though contralateral rigidity was also present, but to a less degree.

(2) *Inhibition of extensor tone.*—Extensor rigidity could be inhibited by stimulating at the following points: (1) the cut surface of the frontal lobe; (2) the mesial side of the anterior limb of the internal capsule; (3) the mesial side of the cerebral peduncle; (4) the brain-stem just posterior to the anterior corpora quadrigemina. In the first three cases inhibition of rigidity appeared on the contralateral side, in the fourth case on the ipsilateral side. If extensor rigidity was present, cutting the middle cerebellar peduncle abolished the possibility of inhibiting the rigidity by stimulating at points (1) and (2) on the opposite side to that on which the peduncle was cut.

Ether rigidity could be inhibited by stimulating the intact frontal area on the mesial side of the anterior limb of the internal capsule. The effect was contralateral.

The experimental evidence, therefore, shows that there are tracts in the brain of the cat carrying impulses which tend to inhibit tonic extensor activity, and that decerebrate rigidity results when the influence of the tracts is cut off. The tracts have their origin in the frontal lobes of the cerebral hemispheres. It is to be noted that the tract on one side of the brain does not govern one side of the body exclusively, since there is an increase in tone on both sides of the body after removal of one frontal area, but the effect is predominant on the contralateral musculature. From the frontal lobe the tract passes through the mesial part of the internal capsule and extends caudad past the level of the anterior corpora quadrigemina. It then, in the greater part at least, crosses to the other side of the brain-stem to enter the cerebellum by way of the middle cerebellar peduncle. The tract thus marked out experimentally agrees in general with the so-called "cortico-ponto-cerebellar" path (Ranson, [6], p. 325).

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THE SENSORY ACTIVITIES OF THE SKIN FOR TOUCH AND TEMPERATURE.

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IT is a well-known physiological observation, that if the end of a slender metal rod, cooled or warmed to a suitable temperature, be applied lightly to the surface of the skin, a sensation of cold or of warmth is not produced at all points of the surface, but only when the point comes into contact with isolated areas, usually of small size. From the surface between these points a punctate cold or warm stimulus produces no sensation of temperature, and touch alone is felt. The responsive areas or points are known as cold and as hot spots respectively.

Similarly, if the surface of the skin be carefully examined with a fine bristle, pressed lightly to elicit the sensation of touch, or with a firmer bristle, pressed more firmly so as to produce pain, the sensation of pain and of touch are not felt equally everywhere but are especially elicited at small spots termed touch and pain spots.

Based upon such observations, the current view of cutaneous sensation regards the surface of the skin as "a mosaic of tiny sensorial areas each sensitive to a specific stimulus, and the range of ascertained sensitiveness includes the sensation of touch, pain, cold and warmth" (Sherrington [7]).

The discovery by Blix [1], corroborated independently by Goldscheider [3], of this punctate distribution of thermal sensibility was by these writers regarded as an illustration of Johannes Müller's law of the specific energy of nerve fibres applied to cutaneous sensation, and led to the belief in the existence in the skin and subcutaneous tissues of specific structural mechanisms, each subserving one or other form of sensibility, whether of touch, in the form of Paccinian and Meissner's corpuscles, or of cold or warmth, for which other forms of end-organs have been stated to act as receptors.

The theory of special end-organs implied also the existence of special nerve fibres connected with them, and the present view of cutaneous

sensation postulates the existence of pain fibres, of touch fibres, and of warm and cold fibres, passing from the special end-organs to the central nervous system.

Sections have been made and examined microscopically of such spots, or fragments of skin which were known to be sensitive to special stimuli, but such search has hitherto failed to demonstrate the presence at such spots of specific end-organs.

The cases of the loss of one or other of these forms of sensibility occasionally found in various regions of the body in syringomyelia and some other spinal conditions, such as a loss of temperature sensation, the loss of touch, or of pain, afforded apparent corroboration of the existence of these separate systems.

Head and Rivers' [4] observations upon the loss of sensation following division of a cutaneous nerve and during its restoration, showed that after such an injury all forms of sensation are not equally lost and are not uniformly restored. Their observations led Head and Rivers to put forward their theory of a dual mechanism of cutaneous sensation, the epicritic and the protopathic, each subserving certain forms of sensation and with special receptor organs and fibres for different forms of sensation.

They deny, however, the existence of a punctate mechanism for all forms of sensation, for in writing of temperature sensation they state that "in the normal skin the hot and cold spots are nothing more than minute areas peculiarly sensitive to either heat or cold, set in a territory over which temperature stimuli can also be appreciated."

The existence of special receptors and special nerve fibres for each of the classical varieties of cutaneous sensation, touch, pain, heat and cold, cannot be considered to be proved, and indeed there are many features of sensation which throw doubt upon the existence of such a mechanism.

In a prolonged series of observations undertaken at the suggestion of Sir James Mackenzie, we have been able to confirm certain facts already known or suspected, and we have observed some others which throw considerable light upon the problem.

The methods employed have been described in the Reports of the St. Andrews Institute [9].

Touch and its Receptor.

Light touch can be excited from all portions of the surface of the body, as well as from certain mucous membranes, such as the conjunctiva

and the buccal mucosa. As is well known, it is best elicited in a pure form by contact with a fine brush or wisp of cotton wool, while on hair-containing parts the movement of a hair sufficient to cause motion of the portion embedded in the hair follicle gives the characteristic touch sensation.

Deformation of the surface is believed to be the stimulus effective for the production of the sensation. Examination by the binocular microscope of a portion of skin while it is being stimulated by a fine bristle, so as to produce the touch sensation, shows that the deformity necessary is of the very slightest character, and almost imperceptible. By such examination the surface of the epithelium is seen to have a somewhat unexpected character; it might be supposed that the surface would show a certain rigidity, but in response to a light touch it is seen to be very mobile—e.g., over the tips of the fingers—and its surface behaves like an extremely thin membrane floating upon a fluid.

Differences of opinion exist as to the mechanism of touch receptors, but it is usually stated to be a function of specific "tactile corpuscles" and their nerves, while the inter-epithelial nerve fibres are stated to convey impulses which give pain sensation.

The terminal branches of superficial nerves end, some in certain specific end-organs, while others pass to the epithelium and terminate among or even in the cells of the deeper layers.

It seems advisable to describe shortly the position of some of the common "end-organs." There are, in man, probably no "end-organs" in the epithelium of the skin, the only form of end-organs which have been described as occurring in epithelium being the Merkel's "touch cells" in the snout of the pig.

These touch cells are large vesicular cells, probably epithelial in origin, lying in groups in the deeper layers of the epithelium, and with a network of neuro-fibrils in close relation to them.

Apart from these, the epithelium is richly provided with nerve fibres, which ramify and form a plexus in its deeper layers.

Nerve impulses are not readily produced by direct mechanical stimulation of nerve fibres; under ordinary conditions they are produced by the activity of receptor organs, and the arrangement in the skin suggests with the greatest probability that touch is not excited by direct mechanical stimulation of these fibrils by deformation of the surface, but that the epithelial cells are receptor organs, which are excited by contact and transmit to the nerve fibrils a stimulus which originates a nerve impulse in them.

The "touch corpuscles" of various types lie for the greater part in the subcutaneous tissues (Paccinian bodies), &c., or in the true skin—and of the latter group, Meissner's corpuscles lie most closely to the surface, occurring as they do in certain of the papillæ of the skin, while other papillæ contain capillary loops.

The distribution of such bodies shows conclusively that they cannot be the sole agents to act as receptors for touch.

Meissner's corpuscles are far too widely scattered in many regions to afford the necessary mechanism—for example, on the volar surface of the forearm one such body was found by Meissner present in 35 square millimetres.

The Paccinian bodies are still less fitted to perform such a function, and their distribution suggests an entirely different use. They are found sparsely scattered in some superficial regions, and exist in considerable numbers in such tissues as periosteum, in the mesentery of the cat, &c., regions from which tactile sensation is entirely absent.

We examined the sensory activity of the exposed surface after removing different thicknesses of skin by blister. The pellicle of a blister is composed of a variable thickness of epithelium, including the stratum lucidum and more or less of the underlying layers. After a short application of a fly blister and in "occupational" blisters the pellicle may contain only the more superficial layers, but after prolonged application the greater part and even the whole of the epithelium may be removed.

When a distinct film of epithelium is left, the exposed surface is dry, and touch can be felt from it, but when more of the epithelium has been removed and the surface is raw and moist, no tactile sensation can be elicited, and pain only is excited by the stimulus.

The inference from the structural and from experimental evidence is that the epithelium of the skin is the receptor organ for the sensation of touch, performing the function of transmitting the stimulus excited by touch to the nerve terminals which are found among the cells of the deeper layers.

Temperature Sensation.

The activity of the cold and warm spots presents peculiar features, some of which have been from time to time recognized by various observers. The first peculiarity to present itself is the extreme difficulty found in enumerating the number of responsive spots present in a given area.

Goldscheider [3], who has been probably the most extensive writer on this subject, has pointed out that at a single sitting a true picture of the temperature spots is not obtained, but that the examination must be carried out for several days if all the spots are to be discovered.

Boring [2] states that it is one thing to map an area in a single investigation for cold or warm spots—it is quite another thing to find these spots a second time and not to find new ones.

The same difficulty was encountered by Trotter and Davies [8] in their observations upon cutaneous sensation in connection with the division of nerves, and Head and Rivers [4] have drawn attention to the varying number of such responsive spots at different observations. Closely connected with this is the variability of situation of the spots, and their ready exhaustion by stimulation.

Our observations established the following facts:—

(1) In different persons there is a very wide difference in the number of cold and warm spots which can be detected at any one observation. In an area of the same size (5 cm. by 2·5 cm.) it was found, for example, in one person that the number of cold spots which could be made out at a single examination varied from eight to eighteen, while in another the number was as great as sixty or seventy.

This difference in number was constant among the individuals, that is, in persons of one group the number was always small, in the other large, but could not be associated with any other condition. The relative numbers of the warm spots followed the same ratio.

(2) Repeated observations corroborate very completely the statement that one or two observations do not disclose the full number of spots within the area from which sensations of cold and of warmth can be elicited, and the sum total of the spots elicited by a number of investigations is vastly in excess of that found at any one time. In other words, under ordinary conditions, of the spots which are capable of giving the thermal sensation, only a fraction are active at one time.

(3) The spots are readily exhausted by a repetition of the stimulus. This is an important phenomenon, but of greater importance is the observation we have made, that dulling of one spot is accompanied by the awakening to thermal sensibility of an adjacent spot. If the point of a fine metal probe cooled to the requisite degree is brought into contact with a cold spot, and the touch repeated again and again at intervals of about a second, at first the contact produces a clear and distinct sensation of cold. After a few contacts, however, the sensation of cold is no longer excited by the stimulus, but that of touch only. The cold sensation may disappear after two or three contacts, or only

after some eleven or twelve, and it may disappear and then reappear once or twice and finally disappear.

If now the stimulus point be moved slightly to one or other side, the sensation of cold is at once set up from a spot from which before no such sensation was elicited.

The Punctate Distribution and "Fluctuation."

The explanation of this varying activity of the spots constituted a puzzling difficulty until we came to realize that we were dealing with a general character of the physiological activity of organs, namely, that under ordinary conditions the whole of an organ is not in a state of activity, but a small part of it only; that there is a coming and going of activity among the different parts—change from activity to quiescence. This feature we have termed "fluctuation," and recognition of its occurrence affords an explanation of many otherwise extremely puzzling phenomena. Some examples may be given.

(1) Fluctuation is very notable at the margins of areas of anæsthesia due to nerve and to spinal injury. In testing the extent of such an area it is a common experience to find that the margin of the area is not the same on two successive occasions—the margin is not fixed, but there is a zone of varying width at one time sensitive, it may be to all forms of stimulation, while at the next examination it may be insensitive. Perhaps more commonly the reverse is found, and the marginal area, formerly anæsthetic, is on a second examination sensitive.

(2) Such fluctuation is also found very notably at the margins of areas of hyperalgesia, whether cutaneous or deeper, and it is almost the rule to find the margin varying at different examinations. Recognition of such fluctuation in these areas was made by Sir James Mackenzie in 1883 [6], and the first record of it is as follows:—

"Towards the end of January, 1881, the patient became worse. He then exhibited the phenomena of hyperæsthetic bands encircling the abdomen, the hyperæsthetic portion on the left side being broader and a little wider than that of the right. The bands could not be distinctly mapped out owing to the variability of the impressions produced. Thus having enclosed, in ink, spaces where the patient declares he feels the pricking of a pin much less than natural, I proceed to other places. On returning to the first spaces I find from his starting and exclamation of pain that they have become hyperæsthetic. The dulled impressions are all either in the upper part of the hyperæsthetic area or slightly above, where they occasionally intermit with the natural about the level of the ninth rib on the left side and the tenth on the right.

"I have been unable to map out the areas on account of the extreme variability of the impressions."

(3) Sensory change and capillary change. The changes in the sensory activity of the "spots" suggested to us that there might be an associated variation in the capillary field. Evidence of the occurrence of such variation is easily obtainable in the condition, common among young adults, in which the fingers and hand are of a purple colour, made up of areas of a deep purple, and of smaller areas of a bright pink colour. If the skin in this condition is carefully watched, it will be found that the margins of the areas are constantly changing, the purple areas encroaching upon the pink ones, while the pink areas die away and new ones appear elsewhere.

Under the binocular microscope the purple areas are seen to owe their colour to a network of small venules filled with blood of purplish colour, and few capillaries can be seen. As the colour alters, small bright red capillary loops come into view in places where none were previously visible.

Examination of an area of normal skin showed that the number and arrangement of the capillaries visible in a given area alter with surprising rapidity.

Capillaries visible at one time disappear from view, and other capillaries make their appearance in the space of a few seconds. The occurrence of such capillary "fluctuation" so similar to the fluctuation in the sensory activity of the normal skin suggests with considerable probability that the two phenomena are causally connected, but of this we have not yet obtained definite proof, as the technical details of the experiments necessary to determine it are extremely complex.

(4) The sensation of itching or tickling shows the same peculiarity. If the surface of the skin on the hairless part, for example, on the front of the wrist, is gently rubbed with a bristle, the sensation of tickling is elicited distinctly from some parts and not from others. If one of these sensitive areas is gently rubbed the tickling sensation gradually disappears, but if the bristle is moved to an adjacent area, usually distal, the tickling sensation is again excited in an accentuated degree.

This gives an explanation of why itching tends to spread by scratching, for the scratching excites the sensitive part and its sensitiveness becomes exhausted, while that of an adjacent area is in turn excited.

(5) Alteration of the vascular condition of the skin produces an extreme modification of its sensitiveness to thermal stimulation. We repeatedly observed the effects produced by applying a mustard leaf so

as to cause an erythema on the sensory capacity of the part, and we found its sensory activity for heat and cold greatly altered. Such a reddened area is not hypersensitive to touch with a neutral body; light touch with the point of a pencil, for example, does not cause pain, but the area is extremely sensitive to warmth. Mild radiant heat, pleasantly warm on unaltered parts of the surface, causes at once a severe pain in the reddened areas.

The first effect of a mild erythema is to alter the sensation resulting from stimulation of the hot spots.

A mildly warm point applied to them gives no sensation of warmth, but, instead, one of sharp pain.

In a more pronounced erythema a further change occurs, and, if such an area is carefully examined for warm spots, a central area is found in which every touch of a warm point produces pain, and around this area is a zone of variable size in which from practically every point of the surface contact with a warm point causes a sensation of warmth. The sensation is not produced only from widely separated points, but from the general surface.

The effect of the erythema is to disturb the "punctate" arrangement of warm spots, and instead of discrete and separated sensitive points, all parts of the surface may become sensitive for warmth.

The principle of "fluctuation" affords an explanation of this phenomenon also. The erythema induced by the mustard leaf has excited to activity all the sensory areas, and all of them respond to the warm stimulus. The effect of the mustard leaf is a "stimulation"—a calling into activity of all parts of the organ stimulated which are capable of activity.

Summary.

The principal results which have been reached include the following:—

(1) There is structural and experimental evidence to show that the epithelium of the skin and of certain mucous membranes is the receptor organ for tactile sensation.

It is not merely a protective covering, but the receptor organ for a special form of sensation, viz., touch.

(2) At single examinations hot and cold spots show a punctate arrangement; the number of such spots in an area of given size however differs widely in different individuals.

(3) On repeated examination of the same area, the number of the hot and cold spots is greatly increased, new spots appearing on successive examinations, while many of those formerly found no longer respond.

These observations harmonize with the results obtained by practically all those who have investigated this subject.

(4) In addition, we find that under certain conditions, such as that of mild erythema, the sensation of heat can be obtained from practically all points of the affected surface at a single examination.

It follows from this that all parts of the surface are potentially sensitive to heat, and that there is no structural punctate arrangement of special receptors and special nerve fibres for thermal sensation.

(5) The punctate distribution of sensitive spots found at a single examination is explained by the view that in the skin there is a constant coming and going of activity of the different parts. Other examples of "fluctuation" are afforded by the skin capillaries in normal and in certain abnormal conditions, and the same principle may form the explanation of the variations found in areas of hyperæsthesia and anæsthesia.

To this coming and going of activity we have applied the term "fluctuation."

(6) The erythema produced by the mustard leaf acts upon the heat-receptive areas in such a way as to abolish temporarily this fluctuation and excites all of them to receptivity.

We do not discuss the bearing of these observations upon Head and Rivers' theory of a dual mechanism of sensation, protopathic and epicritic, each subserving various forms of sensation, but, in our view, the different forms of sensation obtained by these observers indicate differences in the physiological activity of a single mechanism rather than the existence of a dual structural apparatus, each of which is composed of different elements.

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[The fluctuation which is described here in the skin capillaries is amply corroborated by the observations of Krogh [5] which came under my notice after our observations had been made and this paper written.

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THE "LAW OF FLUCTUATION," OR OF ALTERNATING PERIODS OF ACTIVITY AND REST IN LIVING TISSUES.

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In the study of disease which is in progress in the Clinical Institute of St. Andrews we have met with conditions which appear to us to be explainable upon the assumption that the units which make up the structure of the tissues and organs of the body show alternating periods of activity and quiescence. The phenomena are most clearly apparent in the case of the nervous and muscular tissues but are found in others, and appear to be the expression of a property which may be common to living matter generally. This property we term "fluctuation," and by it we mean that the individual units of which the tissues are composed are constantly varying between the two conditions of complete activity and complete rest. Each group of units has its period of activity which is followed by a period of quiescence. The active phase lasts for a while and is succeeded by a period of rest during which other groups are in activity. In this way all parts of the tissue or organ take their share in rotation in the performance of its function, and the activity of the organ as a whole is graded by the number of active units brought into play at any one time. Such an alternation of activity and rest in the units prevents their undue fatigue, is economical in the distribution of work and its resulting wear and tear, and at the same time provides a large reserve of units to meet conditions in which excessive calls are made upon the organ.

The "law of fluctuation," as we are in the habit of terming it, appears to us to be a necessary sequel to the law of "all or nothing," a law which the work of Keith Lucas, Adrian and Forbes has shown to be applicable to muscle and nerve. The phenomena are well known, but the full significance of the law of "all or nothing" in its bearing upon the activity of an organ as a whole has not been sufficiently appreciated. Keith Lucas [9] pointed out that the unit of voluntary muscle, the muscle fibre, when in action always gives a full contraction

and shows no gradation, and that the graded activity of the muscle as a whole is effected by the contraction of varying numbers of groups of fibres. Adrian [1] and Forbes [6] have proved that the nerve impulse obeys the same law, the individual nerve impulse showing no sign of gradation. Voluntary muscle is dependent as regards its activity upon nerve impulses which reach it from the central nervous system through its motor nerves. The graded action of voluntary muscle must, therefore, be of nervous origin, and fluctuation of activity and rest in the muscle must be dependent upon a similar fluctuation of activity and rest in the neurones which are concerned in the control of the muscle. The efferent neurones which supply muscle are not automatic, but are actuated, whether voluntarily or reflexly, by nerve impulses reaching them from other neurones. We must, therefore, look to the reflex arc for the explanation of fluctuation in voluntary muscle. The neurones in the reflex arc are conducting elements and are endowed with properties which render it extremely unlikely that they are directly concerned in the production of fluctuation. The receptors which initiate the nerve impulse, the synapses which lie between the neurones in the nervous system and the receptive substance of Langley or the myoneural junction of Elliott, are all parts of the reflex arc which might be subject to influences determining fluctuation. All these structures are specially liable to fatigue and are the parts of the reflex arc which give to the reflex its special characteristics. The increased resistance offered by the receptors to the initiation of nerve impulses, and by the synapses to their passage from one neurone to another, resulting from slight fatigue, may suffice to bring about continual variations in the incidence and outflow of nerve impulses in the central nervous system. Such an explanation of fluctuation seems a natural one, especially when taken into consideration with the important fact that an unfatigable nerve fibre or neurone is served by numerous highly fatigable receptors, synapses and myoneural junctions. The occurrence of fluctuation in the nervous system would seem to be a provision against severe fatigue, and the question at once arises—does a slight degree of fatigue suffice to divert the nerve impulse, or is some other mechanism concerned? Fluctuation is an established fact in many blood-vessels and especially in capillaries. The temporary cessation of capillary blood flow may in some cases be a sufficient explanation of the coming into action and the going out of action of receptors, synapses and myoneural and other junctions. But here again we are faced with the same difficulty as to whether capillary fluctuation is a nervous

phenomenon, or an inherent property of the capillary cell. If the latter property be granted to the capillary cell the same property may also be extended to other living structures.

Capillary fluctuation cannot be regarded as an adequate explanation of fluctuation in the receptors of an extravascular tissue such as the epidermis of the skin. Fluctuation in the receptors of the skin can be readily demonstrated, especially in those which are concerned with the reception and translation into nerve impulses of heat and cold, and on general grounds the occurrence of fluctuation would seem to be far from improbable in all receptors which lie in multiples upon branches of any one afferent fibre. It is well known that many afferent nerves branch abundantly near their terminations in the periphery, and that each branch of the axis cylinder has its own receptor or receptors. This is especially well shown in the free nerve endings in epithelia. Even special receptors may lie in multiples upon branches of the same neurone as is illustrated by the Paccinian bodies in the mesentery of the cat, where the branches can be traced to their endings. In accordance with the law of "all or nothing" the nerve impulses initiated by any one receptor are full-sized nerve impulses in the main axis-cylinder. The simultaneous stimulation of any other, or of all the receptors on the same axis-cylinder, will give no greater individual nerve impulse than stimulation of one alone. Indeed, only one receptor can be effective at any one time, for the nerve impulse from it will, by its refractory period, impose a temporary block upon all the other branches. If the branches are not in action the nerve impulse, as in an axon reflex, must descend along them and so increase the block. The difficulty is encountered that we do not know the rate of discharge of nerve impulses by the receptors, and it may be that multiple receptors can furnish a more rapid succession of nerve impulses than can be initiated by one alone. It is possible that the magnitude and even the character of the end-result of stimulation of the receptors depend upon the number of nerve impulses initiated in the neurone in unit time.

We suggest that the multiplication of receptors and branches of the neurone is necessary for the continued action of the nerve fibre, and that they act as relays for the latter. Some such arrangement appears to be requisite to enable an indefatigable nerve fibre to be associated in function with numbers of readily fatigable receptors. Fluctuation of receptors or groups of receptors may be ascribable to fatigue, or to an inherent property of some part of the receptor whereby an alternation between activity and rest is effected.

A similar argument may be applied to the branching of the dendrons of the neurones which lie in the central nervous system. Some nerve cells, e.g. the cells of Purkinje, have an enormous number of dendrites and synapses, and nerve cells in general appear to form many synaptic junctions with other neurones. Many dendrons run for great distances from the cell body, but whether long or short there is no reason to suppose that they do not conform with the laws applicable to the remainder of the neurone. If the law of "all or nothing" is obeyed by the dendrons, one synapse only, and the dendrite or portion of the neurone upon which it lies, should be effective in conducting the nerve impulse at any one time. The synapse may be excitatory or inhibitory in its effect, but, whichever it is, it appears to be effective for the whole neurone. It appears to us that rotation of function or the relay use of the synapses is probable, and indeed may be regarded as necessary for the prevention of fatigue in pathways through the nervous system which are in more or less constant use. Unless some such mechanism be conceived, the non-fatigability of the neurone would be useless, and the strength of the reflex arc would be that of its weakest unit, the synapse.

All neurones show a similar system of branching at their efferent ends. Such branches are of enormous importance because they distribute the nerve impulses and allow of diverse end-results from the same stimulus, as well as varying degrees of gradation in the same end-result. The branches on the efferent side of any neurone must receive all nerve impulses coming to them from the main trunk, and if their endings are equally subject to fatigue one would expect them to be equally affected, so that fatigue is not a likely cause of fluctuation as far as they are concerned. It is conceivable that local conditions, such as capillary fluctuation in muscle, might determine the activity or non-activity of the myoneural junctions.

The assumption of the occurrence of fluctuation in the receptors and synapses of the reflex arc, or of the physiological nerve unit of sensation, provides a simple explanation of many physiological and clinical phenomena. It helps to explain the adaptation which occurs in the various end-organs of sensation, and the persistence of sensation to a continued stimulus.

Varying degrees of excitation and inhibition by excitatory and inhibitory nerves are explainable in the results they produce by variations in the number of groups of units in the organ supplied being brought into activity or thrown out of activity. Drugs and toxins

which act upon the nervous system exert their influence upon receptors, synapses or myoneural junctions, increasing or decreasing their sensitiveness and so affecting the passage of nerve impulses through them.

As an illustration of the application of the principle of fluctuation we may take the case of a voluntary muscle, such as the diaphragm, which is in continual action. We have no direct proof that fluctuation exists in the diaphragm and in the nervous respiratory mechanism controlling it, but we are of the opinion that its assumption is a necessity. The diaphragm is capable of great variations in the amount of its contraction, as is shown by the different depths of inspiration which are possible. In ordinary or tidal respiration the contraction is relatively small, but according to the law of "all or nothing" each muscle fibre in it, when contracted, is contracted to its full extent, and gradation of contraction of the diaphragm as a whole must be due to the contraction of varying numbers of groups of its fibres. In a small contraction only a few groups are active, and as more groups come into play the contraction of the muscle as a whole increases. It is unlikely that in the small contraction of tidal respiration, the form of respiration which is of most frequent occurrence, the same groups of muscle fibres are constantly engaged. This would result in a very uneven distribution of the work among the muscle fibres of the diaphragm, and also of the nervous mechanism which controls it. For a maximum effort all parts of the respiratory centre and all the muscle fibres would be brought into action, but the reserve units might be rarely or never used unless there is some system of fluctuation whereby all the units take their share of the ordinary work in rotation.

If there is no such thing as fluctuation in the diaphragm, and in the nervous mechanism controlling respiration, the continual use of the same muscle fibres in tidal respiration must involve the continual passage of nerve impulses through part at least of the same neurones in the respiratory centre, and consequently through the same synapses. Unless these are specially resistent to fatigue we should expect them to show its signs, but we know that no fatigue is manifested in tidal respiration. Haldane [7] has shown that fatigue of the nervous mechanism responsible for the control of respiration can be readily brought about by breathing against a resistance. In breathing against a resistance special effort is necessary, which means that more neurones in the central nervous system and more muscle fibres are brought into action. The fatigue which results manifests itself in rapid shallow breathing which may be very persistent. The condition is seemingly

due to fatigue of the synapses upon the nerve pathways in the respiratory centre. The rapid, shallow breathing is explainable on the assumption that the resistance of all the synapses is raised, and afferent nerve impulses in the centre, instead of flowing easily into the efferent inspiratory and expiratory neurones in steady and prolonged alternation, are more rapidly diverted between them.

The occurrence of fatigue from forced respiration, and its persistence when tidal respiration should suffice for the needs of the individual, point to a fatigue of the synapses on the pathways of the nerve impulses concerned in the production of tidal as well as of the deeper forms of breathing. But in tidal respiration the law of "all or nothing" requires the neurones and muscle fibres engaged to have been in full activity, yet no fatigue results. We suggest that in quiet respirations fatigue is avoided in the reflex arc and in the motor nerve endings of the muscle fibres of the diaphragm by the occurrence of fluctuation, there being some mechanism which diverts the nerve impulses controlling respiration to relays of different neurones, and consequently to different groups of muscle fibres. In this way fatigue beyond a certain point necessary to divert the nerve impulses becomes impossible in ordinary quiet respiration. In the respiratory reflex this alternation may be the result of effects upon the receptors, synapses, and possibly the myoneural junctions, in the reflex arcs concerned.

Barbour and Stiles [2] have found evidence that in the sustained reflex contraction of muscle the contraction is maintained by groups of muscle fibres which are continually alternating between activity and rest. Forbes [6] examines this argument in discussing the economy of energy which is a characteristic of muscle tonus, making use of the suggestion that each group of fibres by its activity excites a reflex contraction of other groups in the same muscle, the first group contracted then going out of action because of synaptic fatigue. He states "the fibre groups in this way take up the load in rotation, and, for some reason, by this means attain an economy otherwise impossible." Forbes looks upon this mechanism of rotation as a possible explanation of some of the phenomena of muscle tone, but states that the evidence is insufficient to warrant its acceptance.

It seems to us probable that fluctuation does occur in the maintenance of tone in muscle, and we would ascribe it to alterations in those parts of the reflex arc which are most susceptible to fatigue, namely the receptors and synapses, and possibly the neuromuscular junctions. Fluctuation does not explain the altered metabolism which

Cathcart and Leathes (3) have shown to be a characteristic of tonic as distinguished from the clonic contraction of muscle. The question is not yet settled as to the nature of the muscular contraction in tonus, nor is the exact nature of the nervous mechanism which controls it known.

Fluctuation is very obvious in one form of exaggerated muscle tone which is met with clinically. Irritation of an abdominal viscus brings about a reflex increase of tone in the voluntary muscles of the abdominal wall, which varies from slight resistance of some part of the muscle to the tense contraction of all the muscles of the wall. It is usually, but not always, associated with pain and with hyperæsthesia of the skin or muscle, or both. Fluctuation, as evidenced by a constantly changing area of the hyperæsthesia and of the parts of the muscle contracted, is very common. The phenomena met with are all of the nature of reflex action, and variations in resistance of the receptors to stimulation, and of the synapses on the reflex arc to the passage of the nerve impulse, are regarded by us as the most likely cause of the fluctuation. An increase in the stimulus which excites the condition brings more neurones into action, and possibly increases the frequency of nerve impulses delivered to each neurone by its receptors. The nerve impulses spread in the central nervous system, and may give rise to numerous other reflexes such as vomiting, increased heart rate, alterations in respiration, sweating, pallor, and even shock. The reflexes are usually attended by sensory phenomena of which pain is the most prominent, but depression, nausea, and exhaustion are also common manifestations.

The "all or nothing" law was first established for heart muscle, but it applies to the individual cardiac muscle fibre and not necessarily to the heart as a whole. The heart has a great reserve power of contraction and is not often required to work to its full capacity. That the heart appears to obey the law of "all or nothing" in its contraction as a whole is probably the result of the co-ordination effected by the controlling influences of the sino-auricular node, auriculo-ventricular node and bundle tissue.

Stimulation of the sympathetic nerves of the heart causes augmentation of its beat as well as acceleration. The increased force of the cardiac contraction must be due to the action of the sympathetic in bringing more muscle fibres into activity. Stimulation of the vagus produces varying amounts of decreased force of contraction, and here we have varying numbers of groups of cardiac muscle thrown out of activity.

In auricular flutter and auricular fibrillation the extent of the ventricular contraction may be very variable. An inefficient beat is not necessarily due to little time having elapsed between successive beats, and so having given little opportunity for the ventricle to fill with blood, for it occurs at varying lengths of time after the preceding beat. But if the law of "all or nothing" holds good for the cardiac muscle fibre, the heart can regulate the force of its beat only by utilizing varying numbers of groups of muscle fibres.

The phenomenon is also seen in the "Treppe" or "staircase effect," which is most easily explainable by assuming a gradual calling into activity of an increasing number of groups of cardiac muscle fibres.

We cannot prove that in the ordinary contraction of the heart fluctuation is constantly occurring, but we are of the opinion that it must be assumed. The heart has a great reserve, and it is unlikely that the units which constitute this reserve do not take their part in the routine work of the heart. We assume that there are more muscle fibres in the heart than are at any one time in action when the heart is beating quietly. These muscle fibres take their turn in carrying on the work of the heart, alternating between periods of activity and quiescence. All come into action simultaneously when great effort is necessary, and the occurrence of fluctuation appears to us to be a necessity for the proper maintenance of a sufficient reserve in the heart muscle.

If fluctuation be admitted in the heart, its causation is even more a matter of speculation. The heart differs from voluntary muscle in many ways, and especially in its controlling mechanism. The nodal and bundle tissues of the heart play a part which can in some respects be compared with the myenteric plexus of the alimentary canal. They act as a local controlling mechanism, and are themselves influenced through the central nervous system. It is probably to some local action through the mediation of these tissues that the cause of fluctuation in the heart must be assigned.

It has been mentioned that fluctuation is a phenomenon manifested by the receptors, and this is especially well seen in the study of skin sensation. It has long been known that fatigue of the receptors is readily induced, but that a sensation of heat or cold from a skin surface may last for hours under a continued stimulus. In an investigation carried out in the Clinical Institute, Waterston has found that the heat and cold spots of the skin are constantly appearing and disappearing. The receptors for most forms of skin sensation are situated in the epidermis, and are probably the cells of the deeper layers of this

structure. Apparently these receptors are constantly varying between activity and rest. In some pathological conditions the alternation is even more pronounced. The margin, between skin showing normal sensation and skin showing hyperæsthesia, is a very good example of fluctuation. Sir James Mackenzie [10] called attention to the fact that the margin is continually varying. That its cause may be a local one in the receptors is evidenced by the alterations produced in sensation as a result of conditions affecting the epidermis. The application of a mild irritant, for example, to the skin entirely alters the receptors, and through them the resulting sensations. But the fluctuation of a margin of hyperæsthesia usually occurs as the result of some lesion in the spinal cord, and it may be that the phenomena are in this case due to fluctuation in the synapses, and consequently to a variation in the incidence of the afferent nerve impulses to the special columns which carry them to the brain.

Fluctuation is already recognized in the capillaries of skin and muscle. Krogh [8], to whom we owe this discovery, states: "Every capillary must therefore alternately open and close, and in the resting tissue, which is poorly supplied with blood, the position of open capillaries must be constantly changing, with the result that the whole tissue is uniformly irrigated when considered over a period of sufficient length." The capillaries appear to be to some extent controlled by reflex action through the central nervous system, but can be dilated by local axon reflexes and by the action of certain chemical substances in the blood, such as histamine (Dale [4]). The cause of fluctuation in the capillaries is not fully understood, and there is some doubt as to the relative importance of nerve control and direct action by chemical means through the blood-stream. The capillary cells, or cells of Rouget, are contractile, and from the point of view of the capillary cell its period of activity must be that of contraction during which no circulation takes place through it. From the point of view of the tissue the dilated capillary is necessary for activity, and it may well be that the tissue has the local power of bringing about that dilatation by axon reflexes or otherwise.

The alternation of activity and rest of the capillaries of the glomeruli of the frog's kidney has been noticed by Richards [11]. The glomerular capillaries reunite to form an efferent arteriole which usually supplies blood to the capillaries of the convoluted tubules belonging to the same Malpighian body, so that the glomerulus, when inactive, probably renders the rest of the tubule inactive. Richards states that

the alternation of activity and rest in the glomerular capillaries is an irregular one, and that the glomeruli act independently of one another. The transition from full activity to complete rest is very rapid, the blood flow stops suddenly, and the glomeruli disappear. Richards draws the inference that a local regulatory mechanism must exist analogous to that shown by Krogh to exist in the capillaries of muscle, and states that the intermittence persists after complete destruction of the whole central nervous system. Here again activity of the kidney requires dilatation of the capillaries, that is to say a state of quiescence of the capillary cell. If Richards' observations are correct, that the alternations take place independently of the central nervous system, some local action either of the nature of an axon reflex or of a direct chemical action on the capillary cell must be postulated.

If fluctuation is a universal property of capillaries an important physiological difference is apparent between those organs which are supplied by capillaries and those supplied by a sinusoidal circulation.

The assumption of fluctuation as of normal occurrence in the capillary circulation appears to be necessary to explain the fact that in conditions where there is a universal dilatation or paralysis of the capillary wall the volume of blood is too small for the maintenance of a proper blood-pressure. Heart failure is not infrequent from this cause: the blood stagnates in the dilated capillaries, and the heart ceases to contract because it is obtaining an insufficient supply of blood.

Histological evidence of fluctuation in the glandular secretions is abundant. The pancreas, when fixed during its activity, presents differences in appearance, especially as regards its cellular content of granules, in different parts of the gland. This we regard as an expression of different stages of activity, and the most likely explanation is that not all parts of the gland are in action at the same time. It cannot be inferred that fluctuation in the secretion of the pancreas is dependent upon the nerve supply, for the main stimulus of pancreatic secretion is a chemical one taken to it by the blood-stream. The pancreas, however, has a nerve supply the action of which is not understood. It is possible that fluctuation in the secretion of the pancreas may be the result of fluctuation in the capillary blood supply to the gland, that the nerves of the pancreas are concerned in the process, and that the mechanism is similar to that described by Krogh in skin and muscle. In glands like the salivary, fluctuation, if present, might be expected to result through the nervous system, for the secretion is a reflex process

and must be governed by the laws applicable to nerve impulses set up in receptors and conducted over a reflex arc.

SUMMARY.

The term "fluctuation" is applied to the alternation of periods of full activity and complete rest which appears to be a property of the cell units of many, and possibly of all, living tissues. The possession of this property by the cells which constitute the walls of the capillary blood-vessels has been demonstrated by Krogh, and it has been observed in the glomerular capillaries of the frog's kidney by Richards. Its occurrence in voluntary muscle has been shown by Barbour and Stiles. The condition was noticed many years ago by Mackenzie in the constantly varying borders of areas of hyperæsthesia which are found in the skin in some cases of spinal lesion.

The assumption of a "law of fluctuation" appears to be a necessity in the case of all tissues which are subject to the law of "all or nothing." It is therefore specially applicable to muscle and nerve, the cell units of which, as demonstrated by the work of Keith Lucas, Adrian, and Forbes, are governed by this law.

The law of "all or nothing" demands that each cell unit, when in action, should give its maximal response to any stimulus which is capable of producing a response, there being no gradation in the individual unit between complete activity and complete rest.

Gradation of activity in an organ made up of units subject to the law of "all or nothing" is due to varying numbers of units, or groups of units, being brought into action. The "law of fluctuation" demands an alternation of the units engaged, so that in the performance of a moderate amount of work all parts of the organ participate in turn, first one part and then another taking up the work in rotation. Such a mechanism prevents undue fatigue of the individual units, distributes the work uniformly over the constituent elements of an organ, and provides a reserve of units, all of which can be brought into action simultaneously when the need arises, and have not suffered from long periods of disuse.

Reasons are advanced for the assumption that fluctuation must occur in the receptors and synapses of the reflex arc.

An explanation is offered of the presence of numerous branches on the afferent side of each neurone, and their function is contrasted with that of the branches on the efferent side of the neurone. It is suggested that multiple receptors and synapses are necessary for the economical

use of the non-fatigable nerve fibre. The nerve impulse is initiated by the receptor, and its frequency may be of the utmost importance in the production of the end-result. The branching on the efferent side permits a multiplication of the end-result, and an irradiatiou in the central nervous system which is limited by the resistance of the synapses met with.

The cause of fluctuation is ascribed to the occurrence of slight fatigue in the receptors and synapses, and possibly in the receptive substance between the efferent neurone and the effector organ. In some cases fluctuation may be ascribable to fluctuation in the capillary circulation. The possibility still remains that fluctuation may be an inherent property of the tissue cell.

Examples are given of fluctuation in nerve, muscle, and glands, and its physiological and clinical importance is emphasized.

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HYSTERICAL PAIN.

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EVEN at this date the term hysterical does not have the exact meaning which is desirable in scientific discussion, and still requires to be defined by everyone making use of the expression. All authorities are agreed that an hysterical symptom is one which does not depend on any demonstrable lesion of any part of the body, and that it is psychogenic in origin. It is over the nature of the psychogenic origin that observers fail to agree. Certain neurologists, such as Babinski [1] and Hurst [7], maintain that the hysterical symptom is nothing but the product of suggestion. The psycho-analytic school declare that the hysterical symptom is always a symbolic manifestation of an underlying psychic complex. We believe that, as a matter of fact, careful inquiry into the onset of every hysterical symptom will demonstrate the presence of a suggestion as a determining factor, but that in the majority, if not in all cases, a connection with some sort of complex can be established.

If expressed in physiological terms it becomes more easy to see how this may be. A suggestion, whether it comes from the patient himself or from his environment, is a pattern of stimuli impinging on the receptors of his nervous system. Sherrington [16] has shown that in accordance with the laws of the selective action of the receptors and the various inhibitions and facilitations established in the nervous system, a certain group of neurones will be activated and modified when a stimulus reaches the body. The exact composition of the group is determined as a result of hereditary dispositions and the conditioning which has taken place through life. Under certain circumstances, depending on the relative strength of the stimulus and the synaptic stability of the nervous system, this group of neurones or engram, to use Semon's term, is so modified as to become a persistent entity more or less "closed," that is, not readily modified by future stimuli. This will be specially liable to occur if the stimulus is persistent over a long period. Of such a nature are the hysterical symptoms which occur as

perpetuations of organic injuries. For example, the musculo-spiral nerve is bruised but not divided by an injury in the arm. The result is a temporary paralysis of the extensors of the wrist and thumb. That is to say, a stimulus coming from higher levels which would normally induce activation of these muscles as a constituent part of a motor pattern of behaviour, fails to elicit any response owing to the blocking of conductivity of the nerve. Had the muscles responded and the pattern of behaviour been carried out, their very activity would have provided new stimuli, which would have induced activation of other engrams in a series of associations, whereby thought, feeling and action would result. Theoretically, at any rate, such patterns may be almost limitless in variety. Thus the action of these muscles becomes a small but definite part of the reaction of the whole organism to the environment. But, as has been seen, there is a break in this chain, for conation in respect of these extensor muscles does not occur. This in itself tends to close the whole pattern which requires the action of these muscles, and isolates the engram from activation by efferent impulses from higher, i.e., cortical levels. Some weeks later the nerve has recovered from its bruising, conductivity is resumed and the muscles are capable of contraction. There is no difficulty so far as the peripheral arc level is concerned. The muscles work as individual muscles if they form a link in a spinal reflex which is set off, and react to electricity and so on, but the activation from higher levels is inhibited. The synaptic junctions are no longer permeable under ordinary circumstances, hence "voluntary" movement is impossible. To put it in another way, these particular neurones cannot be activated with others on the cortical level in consciousness, i.e., integrated to form part of a complicated pattern of behaviour or movement as distinguished from a muscular contraction. So hysterical paralysis results.

However, another factor may come in. It may be that this particular paralysis is of advantage to some complex in the patient's mental make-up. Let us make clear what we mean by this somewhat loose statement. First of all what is meant by a complex? A recent discussion on this subject [13] has exposed considerable divergence of opinion, but has disclosed some valuable definitions. Adapting our definition from these we would describe a complex as a persistent but poorly organized or "untidy" system of emotional dispositions about an object, which may or may not be capable of being represented in consciousness, in contrast to a sentiment which is a system well organized and is always capable of being represented in consciousness.

The hysterical symptom within a complex is the result of interaction between poorly organized or dissociated thinking, and poorly organized or dissociated behaviour. This persistence of the complex is important for psychology. Shand [15] speaking of sentiments lays stress on their capacity for persistence and adaptation to different circumstances, as opposed to an emotion which can adapt itself to one kind of situation only. The same is true of the complex, although it can and does grow and decay, and even disappear after a time. The persistence of the complex often determines the duration of an hysterical symptom. The "untidy" organization is important. Pear [12] has laid stress on the unpredictability of behaviour resulting from a complex. In the same way the composition of a complex is unpredictable and it gathers to itself most unexpected patterns, in the form of hysterical symptoms. Shand points out that both sentiments and complexes are not merely associated with a common effect, but are also relevant and subordinate to an end. If these definitions are accepted we can explain more definitely the loose expression we have used above. In view of an end, all patterns of behaviour which subserve that end will tend to become associated with and drawn into the complex, and while the complex is in being that pattern will remain more or less unmodified by stimuli which activate patterns outside the complex. In neurological terms an engram subserving such a pattern of behaviour will not be readily activated by stimuli affecting neurones outside the engram which subserves a complex.

To return to our example: suppose that at the time the nerve is recovering two complexes are struggling for mastery, one representing self-preservation or avoidance of social obligations, and the other representing altruistic behaviour. The continuance of paralysis may be of use to both complexes inasmuch as it is a compromise between the two. Thus activation of the neurones governing movement of the muscles may be inhibited, because stimuli from outside the complex can only with difficulty activate any pattern within it. This accounts for both the stability of the hysterical symptom and the difficulty of cure. Perhaps an example of the use made of an hysterical symptom to solve a conflict between two complexes will make things clearer. A lady was in the throes of a conflict between the complexes representing her religious and social duties on the one hand, and those representing self-indulgence and avoidance of life on the other. So keen had this become that suicidal ideas had arisen in connection with the second complex and caused the most acute distress, such a solution being

incompatible with the religious and social complexes. One day she stumbled over a low parapet, fell and bruised her back. The suggestion that she could not move her legs was accepted and at once drawn into the net of her second complex, for as she lay in bed, a self-satisfied invalid, she exclaimed, "How fortunate this is, I can't possibly get to the window to throw myself out." Complex number two had temporarily won the day and number one was momentarily satisfied, and the inhibition of stimuli which would cause the perfectly healthy muscles to act was most pronounced.

It should be noticed that although an hysterical symptom is drawn into the pattern of a complex to begin with, by the time that complex has ceased to be of importance to the patient's personality as a whole, the hysterical symptom may have drawn other sets of ideas into association with it and formed a new complex round itself, which will not be resolved till the hysterical symptom is removed. For example, a man is thrown into a state of extreme terror by being exposed to a shell explosion, and as the result of the disorganization of his muscular control he develops a stammer. The hysterical symptom was drawn into his self-preservation complex while the war was on and served this, but later a new self-depreciation complex in relation to unemployment grows round the stammer and persists until the stammer is removed. This explains the divergent methods of treatment and their varying efficacy. In cases not associated with a well-defined complex, where inhibition is chiefly due to habit and prolonged failure to elicit response, direct persuasion readily elicits a series of stimuli from higher levels which overcome the inhibition, but in other cases some resolution of the complex may be necessary before simple persuasion can operate and open up the passage.

From the above it is evident that our standpoint as regards the hysterical symptom is, that it is the product of suggestion and a well-defined complex, and that these determine the localization and character of the hysterical symptom.

We believe that dissociation from cortical control is characteristic of all forms of hysterical symptoms, and our present purpose is to show that this is particularly prominent in relation to hysterical pain, and to indicate certain lines of treatment depending on this concept.

We would define hysterical pain as a release phenomenon in which, owing to functional dissociation of cortical control, the more primitive sensory system convergent upon the optic thalamus is unmasked and holds sway.

The etiology and nature of hysterical pain are subjects which have received singularly little attention in literature, whether from writers on pain in general or from those who deal with hysteria, yet there is no symptom which is so commonly complained of or so greatly considered by the patient. The great difficulty of this study is that pain is entirely subjective and cannot be estimated or measured objectively. Even the distressing appearance of those who suffer really severe pain, such as tic douloureux, is not so much due to the pain as to the secondary effects of fatigue and sleeplessness. It must not be forgotten, therefore, that the intensity of pain felt does not depend on the violence of the stimulus to the pain receptors. In cases of gross neurological lesion, such as that which produces the syndrome thalamique of Roussy, the threshold of pain is actually raised in the affected area, but the intensity of pain felt when the stimulus does produce activation is enormously increased. But even without such gross lesions pain perception may be modified. As Rivers [14] has shown, pain perception may be altogether suppressed by the activation of some other pattern. An airman, whose arm was broken by a machine-gun bullet, described how he felt no pain whatever until he had landed his machine.

If a patient complains of pain, can we say it is all his imagination, and that he feels no pain? Writers on malingering recognize this difficulty but base their conclusions on factors pointing to demonstrable organic causes of pain. Thus Jones and Llewellyn (11) state that "the expert should not dismiss an alleged pain as imaginary or simulated till he has excluded the possibility of an organic cause." These authors also discuss hysterical pain as being associated with hysterogenic zones and stigmata of hysteria. We are convinced that such criteria are valueless, and that unless one can discover the patient in actual fraud the subjective description of the patient should be accepted as a measure of the pain he actually experiences. In practice of course it is not possible to relieve the ultra-sensitive person from his aches and pains, and we have frequently to tell him to carry on and not make a fuss, but it is as well to recognize that we are falling back on the rigorous principle of natural selection in which the weakest goes perforce to the wall.

Our next inquiry must be as to the nature of pain and how it is perceived. Like other sensations that have reached the stage of organization which we can recognize in man, pain presents two aspects for our investigation—one affective and the other cognitive. The first constitutes the feeling aspect—it has much in common with the primi-

tive type of feeling of unpleasure (*Unlust*), and is often referred to by the word pain. This unpleasure, as Freud [3] and Fechner [2] point out, represents what they call a state of extreme psychical tension or instability, and this is characteristic of phenomena of nervous activity released from cortical control or insufficiently integrated to involve cortical control. For example, the epileptiform convulsion and the various *délires*, the psychopathology of which is described by Janet [10]. Hence, this view of unpleasure probably explains why even in normal people extremes of other sensations present an affective aspect practically indistinguishable from pain, for at these intensities they are no longer wholly subject to cortical control, and there is over-stimulation of affective patterns at the thalamic level.

It seems probable that in certain cases of anxiety neurosis unpleasure associated with ideas and not with sensation is actually perceived as pain. The cognitive aspect of sensation consists of the discrimination of quality and reference in space which is associated with cortical sensory areas. As a matter of fact, pain is more affective and less cognitive in its presentation than other sensations, and in accordance with this Head has found that pain is practically unrepresented on the cortex, and that superficial lesions of the cortex have no effect on the pain sensation. Subcortical lesions do, however, affect it, and the most striking effects are produced in conditions of the thalamic syndrome of Roussy and Dejerine, in which the fibres passing from the thalamus to the cortex are interfered with. Under these conditions affective reactions of all sorts are released from cortical control. Amongst these are the affective reactions of pain which are felt with unusual intensity. As a result of such a lesion, acute pains are present which are persistent, paroxysmal, and often intolerable, yielding to no analgesic treatment. Head [5] makes it clear that these pains are due to stimuli from some part of the afferent tract associated with pain receptors, and that they are due to an affective over-reaction. Along with Holmes he established that there were two independent mechanisms associated with the production of pain—superficial and deep. All impulses capable of generating pain become grouped together in the same path, and whether they arise in the skin or in the deeper structures, they become arranged according to functional similarity. Then, after a longer or shorter course, they pass to the opposite side of the spinal cord, and the tracts so formed run up to the optic thalamus without re-grouping, although there may be one or more relays of cells. There is evidence to show, however, that the grosser forms of

pain, such as that produced by excessive pressure, may pass by an alternative route.

The function of the optic thalamus in relation to pain sensation is one of great importance, and Head describes it thus: "The essential organ of the optic thalamus is the centre of consciousness for certain elements of sensation; it responds to all stimuli capable of evoking either pleasure or discomfort or consciousness of a change of state. The feeling tone of somatic or visceral sensation is the product of thalamic activity, and the fact that any sensation is devoid of feeling tone (e.g., posture) shows that the impulses which underlie its production make no thalamic appeal." The thalamus undoubtedly represents the highest level of an older (protopathic) system of sensation, which, as Rivers has shown, has been suppressed by and fused with the more recent cortical system. As Head's experiments showed, the function of this older system is restored earlier after lesion of a peripheral nerve than is that of the newer epicritic system. Under these circumstances the response to pain stimuli is characteristic. The pain seems to radiate from the point of stimulus through the surrounding tissues, and its reference in space is vague and inaccurate, though not abolished.

It should be made clear that perception of pain is due to the reception by the thalamus of stimuli from some part of the afferent pain fibres, whether from the end organs in the pain spots in the skin, or in the deeper structures, or as a result of irritation at the level of the dorsal roots, as occurs in meningeal involvement, or at higher levels. Some misconception seems to arise at times from the expression "pain of central origin," used to describe apparently spontaneous pain occurring in certain lesions of the central nervous system. The most notable example of this is met with in Roussy's syndrome referred to above, but Head has shown that these pains are due to excessive affective response to ordinary stimuli of pain, or even of other sensations such as heat and cold. Some doubtful cases have been described in pontine lesions, and there is Mann's classical case where such pains developed after a lesion of the right half of the bulb. This probably has a similar explanation to those cases described by Holmes [6] in association with injuries to the spinal cord, especially in the cervical region. These he ascribed to lesions of the ventro-lateral columns, insufficient to interfere with conductivity but sufficient to modify the impressions that pass through the affected fibres. The so-called spontaneous pains, in so far as they are independent of peripheral excitations, are probably due to the irritative effects of these lesions on the conducting fibres; and the rarity of these

pains probably depends on the infrequency of that type and degree of pathological change that can irritate the fibres and yet not block conduction through them.

As has been said before, the persistence of hysterical pain may be due to the strength of the suggestion, or to the interaction of suggestion with a complex. In either case the pain will be of much the same character, since suggestion is a constant factor. Such suggested pain is usually the sequel of pain due to so-called organic causes, though it may be intensified by becoming the vehicle of expression in consciousness of other affective reactions, and will be of greater or less severity according to the suggestibility of the patient. Suggestions are more readily induced in extrovert or tough-minded persons, and less so in introvert or tender-minded persons, but once the introvert has accepted the suggestion he will tend to brood over it and elaborate it until it becomes a dominant factor in his mind. In both types the readiness with which a person will accept suggestion depends on the inefficiency of integration of his brain patterns, and so pain accepted as a suggestion will not be under proper cortical control.

Hysterical pain may be referred to any part of the body, and may be described in as many different terms as there are qualifications to the word pain. These pains will, however, be affective in character, that is to say their localization will be inexact and their intensity will be out of all proportion to the stimulus arousing them.

It is manifest that it would be profitless to discuss all possible varieties of hysterical pain; all we propose to do is to refer to certain types of pain which present special interest from the point of view of diagnosis, psychopathology or treatment.

Headache.

The only feature common to all forms of headache is pain referred to the head. Certain pains may be described as headache by the patient, e.g., the pain of fibrositis of the scalp above mentioned; but really these are cases with peripheral reference of pain just as much as those cases in which pain is referred to parts of the body remote from the head. Can it be that there is some broad and fundamental distinction between headache and other types of pain?

Hysterical headache is a recognized clinical entity; its protean forms however suggest that description based on situation and type of pain have little or no value.

Behaviour is response of the organism to environment, and as we

have already seen, it is modified by the conditioning of pre-existent patterns and their corresponding engrams. Hysterical symptoms represent responses involving engrams modified through the agency of suggestion and complex formation. The complex itself indicates former responses on the social level. Hysterical symptoms then represent responses at the psycho-social level, and one of the most characteristic features of this type of response is some degree of cortical or subcortical dissociation.

The symptoms of organic disease on the other hand represent response of the organism to internal somatic factors, e.g., inflammatory foci, and a prominent sign that pain is of organic origin is that it has peripheral reference. The response of the organism in cases of organic origin is then at a lower level than in hysteria. It may be described as a response at the psycho-physiological level, and as a rule this latter form of response does not involve any dissociation at cortical levels. Hence relatively accurate discrimination of and spatial reference of pain is present. Should the local lesion produce some degree of toxæmia, interference with the highest cortical levels occurs. Such interference may reasonably be presumed to produce a condition akin to cortical dissociation in some degree.

On this basis of dissociation at cortical levels, with consequent release and enhanced thalamic activity, it is possible to find common ground for all headaches, hysterical, toxæmic, or the exhaustion headache of true neurasthenia.

Pains in and around the head associated with organic lesions, e.g., sinusitis, dental abscess or meningitis, are, in early stages at any rate, clearly circumscribed, that is they have peripheral reference. It is only in the later stages when through fatigue or injury to the cortex cerebri, as in the case of meningitis, that diffuse headache results. This is the stage of dissociation. Even at this stage there may be some vague localization of the headache, corresponding to the vague powers of spatial reference possessed by the thalamus.

Possibly in this conception of cortical dissociation lies the explanation of the functional element in painful conditions generally. We are all familiar with the fact that intense intellectual preoccupation may suppress even severe pain. In this connection, however, the direction of interest is of course important and presents certain difficulties. Concentration of attention upon a vague, uncomfortable sensation may enhance its affective intensity, until it is appreciated as intense pain; whereas, concentration upon some extraneous subject results in sup-

pression of the sensation of discomfort. It must be admitted therefore that partial cortical dissociation may in no way prevent the "self as knower" from directing attention either towards or away from the "self as known."

Certain cases of cortical injury, e.g., by gunshot wounds, which have been associated with well-marked pain, indicate clearly the ebb and flow of peripheral pain and headache, according as the patient's attention is directed towards his symptoms or away from them to his environment. In these cases the evidence of some degree of partial cortical decontrol has been unequivocal.

To abolish entirely the power of introspection, cortical decontrol must be practically complete, as in epilepsy, in which case loss of consciousness results.

The after-headache in epilepsy corresponds presumably with the period of gradual return of cortical control. Partial dissociation is indicated by automatic activities, by drowsiness, &c., while the appearance of headache indicates some degree of re-establishment of higher control, since the patient must be able to direct his attention more or less in order to appreciate the headache.

To sum up then, there are no striking features pathognomonic of hysterical headache; but, speaking generally, it is affective in character and vaguely localized, its severity depends largely on the attention it claims and bears no relation to the intensity of the stimulus, if indeed any stimulus can be discovered. In diagnosis the process of exclusion and considerations of probability must be employed. The psychogenic origin is to be found in suggestion and the interaction of the latter with a complex, while the physiological explanation lies in synaptic dissociation at or near cortical levels, which unmasks the primitive sensory mechanisms of the thalamus.

Painful Scars.

Scars healthy in appearance and not associated with any known pathological condition are not infrequently the seat of pain. On examination such scars often present the usual characteristics of protopathic sensibility. In some cases pain is strictly localized within the scar and a small neuroma can be found; but the presence of the neuroma is sufficient to exclude such a case from the category under consideration.

There is a second class of case which may be associated with areas of protopathic sensibility, and liable to be regarded as hysterical.

Nerve trunks caught in scar tissue may cause areas of protopathic sensibility in the region of peripheral distribution of the nerve. For instance, in one case the ilio-hypogastric nerve caught in the scar of a kidney incision caused protopathic discomfort of a very intense kind over the region of the cæcum. This was cured by division of the nerve high up, but not before the patient had been submitted to an abdominal section for colopexy and a further operation of colectomy was threatened. Somewhat late in the day the possibility of hysterical pain was suspected, and before the patient was allowed to undergo the operation for removal of her colon she was referred for examination from the neurological standpoint and the cause of her pain was discovered. Here, then, is an organic condition liable to be mistaken for hysterical pain.

Passing to true cases of hysterical pain in relation to scars we have to consider:—

(1) Cases in which suggestion plays a large part.

(2) Cases of hysterical perpetuation of pain, originally of organic origin.

Both types are presumably due to cortical dissociation and show the characteristics of enhanced thalamic activity. They show their essential similarity in that one method of treatment can cure both, though the first class of case, that in which suggestion plays a large part, is not infrequently quite easily cured by some gross form of counter-suggestion. For instance, an intensely painful scar following an operation for varicose veins was quickly cured by a superficial skin incision under gas, made ostensibly for the division of a sensory nerve, but no nerve was divided at the operation.

The form of treatment which has been shown to be successful in the treatment of both types of cases referred to above is hyperstimulation of the painful skin area involved. Three typical cases in illustration may be referred to briefly:—

(1) A sensitive skin area on the back of the neck originating from an attack of herpes eighteen months previously; the skin looked normal but was the seat of intense protopathic sensibility and prurigo.

(2) A painful area in the palm of the hand, following a gunshot injury at the wrist which involved the median nerve; this patient could not bear the lightest touch in the groove between the thenar eminence and the rest of the palm. The condition had lasted nearly two years from the date of the injury.

(3) A case of painful leg and foot, with an area of special tenderness in the hollow of the instep, which, though not of the same hys-

terical type as the above, since it resulted from a central instead of a peripheral injury, supports our contention of the similarity of hysterical pain in general, inasmuch as the same sort of treatment is of service. This case started with a typical thalamic syndrome following a gunshot wound of head, necessitating a small trephining operation. The early acute symptoms slowly subsided, but four years later the discomfort was so great that the patient was very lame and had developed a talipes varus to avoid contact between this painful area in the sole of the foot and the ground. There had been a transient hemiplegia, but when the patient came under our observation there were no signs of organic paralysis.

These three cases were all submitted to hyperstimulation of the painful skin areas. The rationale of the treatment was carefully explained to each patient before treatment was actually instituted. An explanation on the following lines was usually employed: "At the time you were wounded, or when you were first ill, the nerves of sensation conveyed messages as far as a low level in your brain. At this level sensation is interpreted very vaguely, simply as pain or something unpleasant. The highest levels of your brain, which deal with fine discrimination of all varieties of sensation, were temporarily put out of action. This state of affairs has continued long after physical recovery of the injury has taken place. Because you dread all sensation coming from the affected area, your brain is still involuntarily blocking the stream of sensation. You must now learn to tolerate all forms of maximal sensory stimuli; by so doing all ordinary forms of stimulation, e.g., contact with the air, with clothes, with the ground, will cease to arouse your attention, much less your fear or dread. When this stage is reached the blocking of sensory impulses to the highest discriminating levels of your brain will have ceased, and once more you will appreciate all sensations at their true value."

We have not found it difficult to get patients to submit to increasing stimulations, provided the treatment is carried out sympathetically and gradually.

The forms of stimulation used have included rubbing, kneading, smacking with the palm of the hand or with leather straps, the faradic brush, catching a cricket ball, skipping or hopping on the tender foot; also extremes of heat and cold, e.g., metallic contacts and hot water.

Results have been decidedly encouraging. In the case following herpes, the patient, an elderly man who was worn out with loss of sleep, found great relief, and in about fourteen days he was sleeping quite well.

The patient with the tender hand was able to catch a cricket ball, thrown hard at him, by the end of four weeks, and he was also able to enjoy sculling exercise on the river.

The patient with the head injury made considerable improvement over about five weeks.

In all we have treated thirty-eight cases with success by this method.

The crude explanation offered above is pragmatically useful in dealing with patients, but it is no easy matter to find a scientifically satisfactory theory to account for the phenomena. Starting from the idea of dissociation of cortical control unmasking thalamic sensibility in the case of hysterical pain in scars, it is difficult to understand why a few weeks of hyperstimulation can secure a more or less complete return of normal sensation in the affected area.

As a rule all these patients are obsessed with their pain and discomfort, and concentrate a great deal of attention upon them, or rather upon means whereby the dreaded pain may be avoided. Apparently this concentration in itself acts as an inhibition, whereby reassociation between thalamic and cortical levels is prevented. It may be that in this method of treatment we are dealing with phenomena closely akin to what obtains in the process of free association in psycho-analysis. This may be clearer if expressed in neurological terms. Deliberate repression by an "effort of will" means that impressions coming from neurones at lower levels are prevented from activating the most highly integrated neurones. As time goes on it is quite possible that this inhibition may take place at lower levels, cf. Hurst's [8] explanation of the abolition of the blink reflex in hysterical blindness, and in cases of unconscious repression, where inhibition may occur at comparatively low levels in the nervous system. However, in such cases as those under consideration, the inhibition occurs at subcortical levels at lowest, and it may well be that the removal of the effort at repression alone does much to remove the inhibition, and with re-education paths from thalamic to cortical sensory levels again become permeable.

Visceral Pain.

Head has pointed out that visceral pain belongs to the protopathic thalamic system, and in consequence its reference is vague and its intensity extreme. It follows, therefore, that in this region hysterical pain does not differ materially from that produced by organic disease. For this reason differential diagnosis presents great difficulties, and

without question this accounts for many surgical operations performed in all good faith for apparently unequivocal symptoms, but which disclose little or nothing abnormal. The only way to guard against such mistakes is the greater exactitude of diagnosis and the education of surgeons to consider mental factors in their patients, for though such operations occasionally do good by suggestion, they more often do incalculable harm. Just as in other parts of the body a definite organic condition is apt to serve as the suggestion which established an hysterical symptom, so in the abdomen it is found that the pain of a duodenal ulcer or an acute appendix will be perpetuated as an hysterical symptom which will persist as a habit pain, or because it is of use to a complex. When this occurs after operation it too often happens that a diagnosis of adhesions is made. Once the patient gets hold of this, the "organic excuse" allows him to rationalize on his hysterical symptom and therefore makes the establishment of proper cortical control more difficult than it would otherwise have been. But it sometimes happens that a second quite unnecessary operation is undertaken to free adhesions, even in the absence of any obstructive symptoms. Needless to say this only makes things worse, and the last state of the patient is worse than the first. Two examples may illustrate how the hysterical symptom may be induced and persist. The first was a man who while in a small tropical station acquired a duodenal ulcer. At the same time he developed a neurosis as a result of various domestic and social maladaptations, which resulted in a marked self-depreciation and dread of going out and mixing with people. He came home and underwent an operation at which the ulcer and all the symptoms except the pain were removed, but for six years he persistently complained of attacks of pain similar to those which he had experienced as a result of his ulcer. On closer investigation it was found that the pains only came on severely when his wife wanted him to go out or social duties called him into the society of strangers. The pain pattern had been drawn into the complex of his self-depreciation, which determined his social behaviour, and whenever this was activated the pain was experienced and proved a useful means whereby this complex controlled the behaviour of the patient.

Another case was that of a boy, who while in France in the line had an attack of acute appendicitis. He had had a good deal of difficulty in sticking it out, and this probably had to do with the fact that after the operation, which was performed in the end of July 1918, the vomiting and pain continued. So violent was this that it was thought that

obstructive adhesions had formed, and in the end of August his abdomen was again opened but no abnormality was found. From this time matters went from bad to worse and he was given morphine for the pain and was fed by nutrient enemata. At the beginning of November, at about the time of the Armistice, he was admitted to a Neurological Hospital and in three days was on normal diet and was suffering no pain. All went well until about Christmas, when he received a letter from a girl with whom he had been entangled before he went to France and from whom he thought he was free. This letter gave rise to serious conflict, as he did not wish to tell his parents about this affair and without their help could see no way of escape. At once he started to vomit again and complained of and obviously suffered severe pain. When urged to face the problem and come to a decision he stated that the pain was so bad that he could not possibly think, but the influence gained over the patient by the previous success of psychotherapy made it possible to get him to give his mind to the problem and solve the conflict next day; with this the vomiting and pain disappeared for good. This is an interesting illustration of how the disorganization of cortical control which resulted from the temporary insoluble but quite conscious conflict allowed the activation of the old engram with its thalamic type of response.

In cases of visceral pain then it is impossible to diagnose whether it is hysterical or not from the type of pain, since all such is thalamic in character, and the diagnosis can only be by inference, both negative and positive. That is to say, by the absence of other symptoms and signs which should be present were the lesion organic, and by the recognition of some foregoing suggestion such as would be likely to determine the pain as an hysterical symptom, or of some psychological reason for the persistence of pain.

It may be well to notice a type of pain which is often referred to as hysterical but which is not really so. This is the pain which accompanies muscular contractures which are themselves hysterical. One of us [4] has described a series of such cases which occurred as hysterical complications of "rheumatic" conditions. "In this state the pain which is present is no longer due to inflammation, but to the cramp produced by the muscles which are being held in a state of abnormal tone, and to the stretching of fibrous tissues and of other muscles, as well as to the pressure which is being kept up on abnormal surfaces in the joints." Such pain then is "organic" in character and exhibits accurate reference and discrimination, and although it disappears as a result of psychotherapy it is not itself hysterical in nature.

The diagnosis of hysterical pain can only be reliably established by a process of exclusion, and while an examination for an organic cause should be thorough it should be carried out as rapidly as is consonant with this thoroughness, and with the greatest care to avoid suggestion; for otherwise not only may an hysterical symptom be perpetuated but the subjective affective element in the pain which is experienced may be increased. The old search for hysterical stigmata is futile and misleading, for, as Hurst [9] and others have shown, such stigmata can be produced as fast as they are looked for. The only positive evidence of hysterical pain which can be relied on at all is, if there has been a strong suggestion to determine the pain, and if the presence of the pain may be of such use to a well established complex as to outweigh the unpleasant feeling induced in the personality as a whole.

With regard to treatment little more need be said here. So far as the suggestive influence is concerned it may be removed by counter-suggestion and re-education, and so far as involvement in a complex is concerned this latter must be resolved by the methods now familiar to all workers in this field. The whole object of such treatment, however, must be to re-establish integration on the cortical level, that is to say, in psychological terms, in consciousness, and we have sought to show that hysterical pain like other such symptoms is a dissociation from this level, and that our object must be to restore integration.

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Proceedings of the Section of Neurology of the Royal Society of Medicine.

Meeting held April 12, 1923.

Pathological Findings in the Central Nervous System of a Case of Myasthenia Gravis.

By Sir Frederick W. Mott, and Dr. Y. A. Barrada.

The patient joined the Army in August, 1914. His illness began in 1918 with weakness of his lower limbs: a very short walk "did him in completely." There followed progressive weakness of all his limbs but no pain or paræsthesia accompanied this. Two weeks later fluid began to return through his nose, his voice became weak, and chewing food became almost impossible. Major Walshe examined him in July, 1918, and found the masseter and temporal muscles exceedingly feeble. There were marked double facial paresis, and paresis of palate, larynx and pharynx. The whole musculature was very weak and readily fatigued. Sensation and reflexes were normal. Myasthenia gravis was diagnosed. On his way back to England he was reported to be liable to attacks of respiratory failure. In September, according to a report of the Medical Officer of the Maudsley Hospital, the patient had partial ptosis of the right eye, his lips parted, and the smile had the appearance of a sneer. He was unable to wrinkle his forehead, close his eyes firmly, whistle or blow out his cheeks; and he was unable to masticate his food. Speech was good in the morning, but towards evening the muscles of articulation tired and the voice became slurred. The intercostal muscles were also affected. He had diplopia which was not constant in position, his knee-jerks were absent, but there was no loss of sensation. On February 19, 1919, the patient had an attack of dyspnœa which continued until death, which took place the same day.

The post-mortem was performed on the same day; the following changes were found.

The thymus weighed more than 70 grammes, and was completely surrounded by a thick fibrous capsule. Microscopically there was no

distinction between its cortex and medulla; the tissue was composed of a mixture of faintly stained epithelioid cells with large vesicular nuclei lying side by side, but a preponderance of lymphocytes varying in density in different places was observable. There were many spaces filled with more or less clear eosin-stained material with some epithelioid cells undergoing colloid degeneration, and a few lymphocytes. These spaces were lined by epithelioid cells arranged in a layer with the long axis perpendicular to the space. Evidence of mitosis could be seen in these epithelioid cells. There were no eosinophil cells, and only a few swollen and degenerated Hassal's corpuscles. The capillary blood-vessels were lined by unbroken endothelium, and contained some lymphocytes.

Muscles.—Numerous foci of lymphocytic infiltration (Buzzard's lymphorrhages), varying in size, were found in the diaphragm, lying between the muscle fibres. The muscle fibres themselves appeared to be normal.

The nerve fibrils and their terminations in the masseter and orbicularis palpebrarum muscles were stained by Dogiel's method with intravitam methylene blue, and appeared to be normal.

Central nervous system.—There was general diminution of the basophil substance throughout the central nervous system. This was most marked in the small and large cells of the thalamus and was associated with vacuolation, eccentric nuclei, invasion by satellite cells and increased neuroglia. Similarly, the third nerve nucleus showed very marked changes, but to a less degree than the thalamus; in the trochlear nucleus they were still less pronounced. The other cranial nerve nuclei as well as the anterior horn cells of the spinal cord showed very little basophil change, although here and there some cells were found with marked chromatolysis, eccentric nuclei and swollen and vacuolated cytoplasm.

With Scharlach and Nile Blue stains, widespread lipoid changes were observed in the cells, and were noted to correspond in their intensity to the amount of chromatolysis, These lipoid granules were also found in the perivascular spaces, which afford a proof of the lipoid change having occurred prior to death. It is noteworthy that the changes observed in the cortex and cerebellum were less pronounced than in the above-mentioned regions.

There was general congestion of blood-vessels, but no hæmorrhages. No lymphorrhages were found anywhere.

Unfortunately no other tissues were obtainable for examination.

As regards the pathogenesis of myasthenia gravis, the view is gaining ground that it is primarily due to some form of autotoxin resulting from a disturbance of the internal secretions or disordered metabolism, which exerts a deleterious effect on the functions of the muscles. An exotoxin seems to be capable of exerting similar influence, since myasthenia has been observed to follow infectious diseases and such poisons as barium salts, chlorine gas, war gas, &c. The fact that in the myasthenic electrical reaction the muscle reacts well to galvanism after complete exhaustion to faradism, suggests that the primary seat of fatigue is at least not limited to the muscle. Further, there is not sufficient evidence, on pathological grounds, to show that the muscles or nerves are directly responsible for the phenomena of fatigue exhibited by the patients in voluntary movements. Considering these facts, and that cellular changes in the nervous system have been described by Kalischer, Widal, Marinesco, Murri, Guthrie, Leclerc and Savornat, it is quite possible that the changes in the central nervous system found in this case may be correlated with the manifestations of myasthenia.

DISCUSSION.

Dr. GORDON HOLMES stated that though he could not doubt the correctness of the observations made by the authors, he could not accept them as explaining the disease from either the pathological or clinical standpoint. In the first place it was surprising that the changes as were here described have not been detected previously in the large number of cases of myasthenia gravis which had been examined by competent neuro-pathologists. In the second place he did not see how the clinical phenomena of the disease, and especially the localized muscular disturbances which were present in many cases, could be explained by them. He pointed out that single muscles or irregular groups of muscles only might show prominent changes, such as orbicularis oculi or oris, or as in a case at present under his care the triceps, and asked how this localization could be accounted for by such a diffuse and general affection of he central nervous system, for cerebral affections lead to disturbances of movement and not of the functions of individual muscles. It was also striking that despite such changes the symptoms were practically limited to the motor system. It seemed to him that all the pathological findings which had accumulated during the last twenty years, since Weigert originally pointed out the association of myasthenic symptoms with tumours, hyperplasias or persistence of the thymus gland, indicated that disturbances of the normal functions of this gland must play an important part in the pathogenesis of the symptoms. In six of the eight cases which he had himself examined by autopsy there were either tumours or enlargements of the thymus. It seemed to him that it was only from further studies of the physiology of the thymus that we could expect much light on the pathology of this disease.

Dr. WALSHE asked how Sir Frederick Mott would explain the absence of mental and other symptoms if the lesions of the central nervous system which he and Dr. Barrada had described were of pathological significance. He felt convinced that the paper threw no light on the nature of myasthenia gravis.

Dr. GREENFIELD also insisted on the importance and frequency of tumours and the enlargements of the thymus: negative observations seemed to him of little value unless the mediastinum was carefully and systematically searched, since thymus tissue could be easily overlooked in the fat of this region. In three cases on which he had recently performed autopsies the thymus was persistent, and though not much enlarged each consisted of glandular tissue and was obviously functional. Microscopical examination revealed proliferation of the epithelioid cells, which in places seemed to be going on to the formation of Hassal's corpuscles. It is difficult, however, to say whether these changes in the thymus are primary, or secondary to the disease of some of the other endocrine glands. He has failed to find any lesions in the parathyroids that could support Chvostek's hypothesis. In one of his cases there was certainly no excess of lipoid, such as has been described by Mott and Barrada, in the nerve cells.

Dr. SYMONDS referred to some ergographic observations he had recently made, which could be most easily interpreted by assuming a lesion in the nervous mechanisms of movement. First, he determined the strength of a faradic current necessary to produce a brisk response of a muscle; then he exhausted the muscle by voluntary contraction, and when it no longer contracted to voluntary stimuli he found that he could immediately obtain an undiminished response to the same strength of faradic current. He also referred to the pains and other sensory symptoms that are occasionally observed in the disease. He described a case which had recently died under his care, in which, in addition to weakness of the muscles of the jaw and of the external ocular muscles, clonic twitchings of the right limbs and disturbances of speech occurred. There was also loss of taste. This patient had very severe dental sepsis and he suggested that toxins carried from the mouth to the brain may have induced the changes which excited symptoms of the disease. Post-mortem examination revealed an enlargement of the thymus and cellular infiltration of the muscles.

Dr. BIRLEY said that it seemed to him that there was no evidence that the case referred to by Dr. Symonds was one of myasthenia gravis; it was much more probable that the so-called myasthenic symptoms were due to a neuritis of the cranial nerves.

Dr. FEILING stated that he discovered no enlargement or persistence of the thymus in three cases on which he had made post-mortem examinations, though the effect of pregnancy on the disease suggested that some endocrine disturbance played a part in it at least.

Sir FREDERICK MOTT in reply pointed out that he did not regard the changes which he and Dr. Barrada had discovered in the central nervous system as definitely proven to be the cause of the disease, though they were certainly

significant. He could not deny that the frequent enlargement of the thymus was important, but its exact cause was still a matter of doubt; it may be only the effect of a general endocrine disturbance.

CLINICAL MEETING HELD MAY 10, 1923.

By Dr. A. FEILING.

(1) *Case of* (?) *Progressive Double Athetosis.*

A boy, now aged 9, was a normal child at birth, and so continued until August, 1919, when, as the result of a street accident, he had his right foot amputated. After recovery, and when he began to use crutches, involuntary movements were noticed in both arms. Later these movements affected the legs as well. Three years ago dribbling from the mouth began, shortly followed by a progressive loss of speech. Until about eighteen months ago he was able to swallow well, but in the last year spasmodic movements of the jaws have seriously interfered with feeding. The mental faculties have not suffered. He has had measles, chicken-pox and erysipelas. No history of any nervous or mental disease in the family; there are three other children alive and well; one child died of pneumonia, and there was one miscarriage three months after marriage.

On examination the child is undersized. He is now quite unable to speak, but he can indicate by signs what he means and is perfectly intelligent, though the mental state is retarded for his years. Pupils and optic discs normal. No paralysis of the ocular muscles or of the face. Constant spasm of the jaws leading to marked grinding of the teeth and interfering with feeding and mastication. The tongue can hardly be protruded at all, and, when it is, is deviated to the left. Swallowing is very difficult and food sticks in the throat.

The arms, and especially the left, are the seat of involuntary movements. These take place at all the joints, but are most marked at the shoulders. They are more of the type of athetosis than anything else. There is no actual paralysis. There is not much alteration in the muscular tone, though, perhaps, some hypertonus is present. The arm-jerks are present. Similar movements affect the legs, but the right more severely. The knee-jerks and the left ankle-jerk are active. The left plantar response is somewhat doubtful, probably flexor. No loss of sensation has been found. He is quite unable to stand even with assistance and a peg leg, and now cannot sit up unaided.

One year ago the Wassermann reaction in the blood was feebly positive, but the cerebrospinal fluid was quite normal. The Wassermann in the blood of the mother is negative. He was treated a year ago with antisyphilitic remedies, mercury and iodide and intramuscular injections of glucarsenol. Some improvement took place, but recently there has been a slow deterioration, especially in the power of swallowing.

(2) *Case of Chronic Mercurial Poisoning.*

By Dr. E. A. CARMICHAEL.

Patient, a male, A. S., aged 51, thermometer maker.

History: Eighteen months ago teeth became black and loose. Twelve months ago gums were painful. Three months ago salivation and unsteadiness of hands with "trembling" of legs. Two months ago difficulty in going upstairs, followed later by weakness in wrists. Seven weeks ago bad occipital headaches and aching in knees and wrist. Looseness of bowels of indefinite duration. During the last three months memory has been very bad and speech slurred. No history of stabbing pains, vomiting, delusions or obnoxious taste.

On admission: Skin of body, and especially of face, dirty sallow colour. Teeth few in number, black, loose with retracted gums. Tongue raw looking. Arteries slightly thickened. Fundi normal. Pupils equal, no ocular abnormalities. Lower jaw trembling as if silently mumbling. In the hands and legs similar irregular tremor. Grasp poor, extensors of wrist weak. Plantar flexion of both ankles weak. Reflexes normal. Diminution to pinprick and cotton wool of glove distribution on arms, over legs and on the lower trunk. Blood count and picture normal. Gastric contents showed diminution of free HCl. Cerebro-spinal fluid and blood normal.

The patient has improved considerably since admission.

(3) *Case of Muscular Atrophy of the "Peroneal" type apparently commencing in, and confined for some time to, the right hand.*

By Dr. C. P. SYMONDS.

The patient, Mrs. C., aged 32, belongs to a family in which I have found nine members affected by the disease in two generations. She belongs to the senior generation, and her father is also stated to have suffered from the disease. Her sister, Mrs. B., aged 38; her niece, Miss B., aged 15; and her nephew, Mr. William C., aged 17, are presented as typical cases of peroneal muscular atrophy.

The present patient, Mrs. C., states that she has noticed from childhood that the fourth and fifth fingers of her right hand would not straighten out properly. She has never been seriously inconvenienced by weakness of either hand. She was at school till the age of 14, then in domestic service for six years, married at 23, and has two children aged 8 years and 2 months, whom I have seen, and who appear in every respect normal. The deformity of the right hand was recognized by the family from childhood. She states that she has suffered from no illnesses except occasional headaches, and that she has noticed nothing wrong with her feet.

Her general condition is good, and her mentality normal. The right hand shows wasting of the intrinsic muscles of moderate degree. This is essentially of the ulnar type. The intrinsic muscles of the thumb are slightly, if at all,

affected. The hand is deeply hollowed, the hypothenar eminence is lacking, all the palmar and dorsal interossei are wasted and weak, the wasting and weakness roughly corresponding. The left hand is relatively normal. Both feet show pes cavus with claw toes. This is of moderate degree and more pronounced on the right than on the left. Power in the feet and legs is good on the whole, though dorsiflexion is somewhat weak on the right. When examined a month ago fibrillary twitching was noted in the peronei of both legs, being more noticeable on the right. Sensation to cotton-wool and pin-prick is normal, but sense of position is slightly impaired on the toes. Sensibility to the vibrating tuning-fork estimated quantitatively appears diminished both in legs and arms. The ankle-jerks could not be obtained; knee-jerks sluggish, obtained only with reinforcement; left triceps-jerks greater than right; supinator-jerks not obtained; abdominal reflexes present and equal, and the plantars indefinite.

DISCUSSION.

Dr. STANLEY BARNES referred to a series of cases in which he had found a somewhat similar type of myopathy. In this series there was a strong inheritance, the disease could be traced back in the family as far as 1804. One of the most unusual features was the degree of variation at different periods of life, so that some of the cases appeared at one stage to be of the true hypertrophic type, at another of the juvenile type, and in one case at a late stage it might have been thought that the patient was suffering from the distal type of myopathy. He expressed his interest in these cases, and hoped it would be possible to publish both series at the same time.

Dr. F. J. NATTRASS said he had recently seen two cases of this disease in brothers, both of whom had double drop-foot due to wasting and weakness of the anterior tibial groups of muscles, but in both the peronei still retained good voluntary power. Strong faradism failed to elicit any response in the tibiales antici, but the response of these muscles to galvanism was almost as brisk as normal. The peronei contracted well to faradism.

(4) *Case of "Juvenile" Tabo-paresis.*

By Dr. C. WORSTER-DROUGHT.

R. P. B., MALE, aged 26. No history of any illness of importance before onset of present disorder. Was up to the average standard at school; on leaving, worked as a "light porter" in Government service until his mobilization with Territorial Forces in August, 1914. In January, 1917, he appears to have had a "seizure," and, as a result, was discharged from the Army in May, 1917. He returned to his civil employment and continued until 1919, when increasing mental deterioration and the fact that "he was always falling asleep" led to his dismissal.

Present condition: Invariably cheerful and self-satisfied; childish and inane, but usually answers questions fairly rationally; inclined to be grandiose

in his ideas with some degree of confusion ; memory for past events very poor and orientation fairly good. No delusions. Both pupils irregular in outline with no reaction to light, direct or consensual. Optic discs somewhat pale. Hutchinsonian teeth. All arm-jerks brisk, knee- and ankle-jerks absent. Ulnar nerve and tendo-Achillis analgesic. Frequent urinary incontinence. Some unsteadiness of gait and Rombergism, but not marked. Wassermann reaction positive in the blood. Cerebro-spinal fluid (last examination) 272 lymphocytes per cubic millimetre, globulin and Wassermann reactions positive, colloidal gold curve of " paretic " type.

Under observation and treatment with novarsenobillon intravenously and mercury cream intramuscularly at intervals during the past four years, patient has shown very little change, excepting for a steady increase in the cell content of the cerebro-spinal fluid, from 88 cells to 272 cells per cubic millimetre.

(5) *Case of Juvenile General Paralysis of the Insane.*

By Dr. C. WORSTER-DROUGHT.

C. M. D., MALE, aged 22. Patient left school in Standard VI at the age of 13, having had no illnesses except attacks of bronchial catarrh each winter. When he was 14 years old he began to " stammer," but was able to carry on with his work until he was 18 (four years ago) ; he then had a " fit," and was unconscious for twelve hours. Since that time he has steadily deteriorated, both mentally and physically. His father died sixteen years ago (aged 40) from pneumonia, while his only brother, aged 15, has interstitial keratitis. His mother is alive and well.

Present condition : Mentally dull and stupid, and easily amused, but occasionally he answers questions fairly intelligently. Both pupils inactive to light, direct and consensual ; optic discs not unduly pale. Arm-jerks brisk and equal, abdominals brisk and equal, knee-jerks both present, ankle-jerks unobtainable, plantar reflexes flexor. No ulnar nor tendo-Achillis analgesia. Gait uncertain and unsteady but no Rombergism. Wassermann reaction positive in the blood. Cerebro-spinal fluid (last examination) 82 lymphocytes per cubic millimetre ; globulin and Wassermann reactions positive.

During the past three years he has been treated with courses of novarsenobillon intravenously and mercury cream intramuscularly ; the only changes are increasing tendency towards dementia and loss of ankle-jerks.

(6) *Case of Huntington's Chorea.*

By Dr. C. WORSTER-DROUGHT.

J. T., MALE, aged 45, complains that he " cannot keep still," the continual movements resulting in insomnia. The condition developed in 1917 while the patient was serving in France, but he was able to continue in the Army until 1919. In spite of a variety of forms of treatment the movements persist unchanged.

Present condition: If observed he is seen from time to time to exhibit jerky movements of the head and limbs; the neck is jerked backwards, the back straightened, and the head then falls forwards, and the back becomes bowed. The hands may be thrown to one side with the whole arm sweeping outwards; while sitting he has found that his feet are continually shuffling owing to the leg movements. All the movements are loose, jerky, and show a wide excursion. It is understood that his wife is "always grumbling because he moves about so much in his sleep." Under hypnosis the movements continue, but are less pronounced. Mentally, he is irritable, depressed, and his memory for past events very poor. Speech is indistinct, and somewhat grunting in character, and is often accompanied by lateral movements of the head. The pupils, fundi and other cranial nerves show no abnormality, the knee- and ankle-jerks are active, and the plantar reflexes flexor. Wassermann reaction is negative in the blood. Cerebro-spinal fluid: two cells per cubic millimetre; Wassermann negative; globulin slight increase; colloidal gold reaction "luetic" curve (0.1.1.1.1.2.2.1.1.0).

Family history: Nothing of importance can be traced. He has been married six years and has no children. His mother died when he was 14 (thirty years ago)—of what disease he does not know—and his father as the result of an accident twenty years ago. He has a brother, three years older than himself, and a sister three years younger, both alive and well.

(7) *Case of Quadriplegia with Traumatic Spondylitis.*

By Dr. DOUGLAS MCALPINE.

M. D., FEMALE, aged 42, was well until February, 1921, when she fell into an area. She immediately lost consciousness. Later she found she could not move her head or any of her limbs. She had retention of urine. At end of one week power began to return in left arm, and gradually the other limbs recovered, but a general weakness has remained, this being most marked in her right arm. Since the accident she has suffered from shooting pains across the back of neck and down both arms. She has shown progressive improvement whilst under observation.

Examination shows nothing abnormal in the cranial nerves. No localized wasting in shoulder or arm muscles. No sensory disturbance in limbs or trunk. Moderate loss of power in both arms, in the right more than the left. Tone in right arm is increased in triceps and flexors of the wrist. Posture of right arm when walking is one of extension at the elbow, pronation of the forearm, flexion at the wrist. No material change in tone or posture in left arm. Tone in the lower limbs is slightly increased in extensors, but power is quite good. Deep reflexes are much exaggerated in arms and legs, but more so on right side. Right plantar response is extensor, while left is equivocal.

X-ray examination shows bony outgrowth from third, fourth, fifth and sixth cervical vertebræ.

(8) *Case of Syringomyelia with Pain of Central Origin.*
By Dr. A. G. DUNCAN.

W. M., MALE, aged 37. Fifteen months ago he first noticed a weakness in his left arm, which has gradually progressed. Pain was also experienced in left arm, and later in left upper chest and left side of the face and this has persisted.

Examination shows hyperæsthesia to cotton wool and pinprick, with partial loss to heat and cold in distribution of left fifth cranial nerve. In addition there is moderate loss to all forms of sensation on left side of neck, left arm and left side of the trunk, extending down to the level of eighth dorsal segment. The loss of postural sensibility is very marked in left arm. Nystagmus present. No involvement of other cranial nerves. No muscular atrophy left arm. Deep reflexes more active on left side, and left plantar response is extensor in type. There is no loss of sensation in left leg or on trunk, or in the limbs on right side.

(9) *Case of Right Frontal Tumour; Cracked-pot Percussion Note over Right Frontal Bone; Left Palmar Reflex.*
By Dr. GEORGE RIDDOCH, and Dr. BRAIN.

W. G., aged 8, Hebrew boy, left-handed and a twin, was noticed six months ago to be weak in the left hand: this has become progressively weaker. He has complained of headaches, beginning in the right temporal regions, for four months, and has vomited every few days for the same period. His face was noticed to be "on one side" two months ago; and there is a history of occasional stammering and some indefinite visual impairment.

On examination on February 20, 1923, there was a visible boss on the skull in the right temporal region, divided by the right fronto-parietal suture. On percussion a cracked-pot sound could be elicited over the right frontal bone while the left yielded a boxy note. The fundi showed blurring of the edges of both discs with one diopter of swelling in the right. There was a left hemiparesis, the weakness affecting the facial movements most, the arm to a less extent, and the leg only slightly. Sensation was normal.

A fortnight later small clonic movements were observed in his left face and arm, and in his right leg.

Palmar reflex: It was noticeable that objects placed in the left hand were the more strongly clenched the more one attempted to pull them away. This reaction can still be obtained, and is evoked especially by moving contact from the flexor surface of the fingers and especially of the first finger and thumb. The reaction is entirely involuntary, for the patient obviously makes strong efforts to relax his grasp. He is usually unable to extend his fingers, but the reflex can be well evoked even when spasm of the fingers is largely eliminated by passive flexion of the wrist.

At the present time there is some loss of postural sensibility in the fingers of his left hand. Tactile discrimination, localization and sensibility are also defective in the left upper limb. There is now some secondary atrophy of both optic discs.

Meeting held June 14, 1923.

Hysterical Fits, with some Reference to their Treatment.

By Dr. L. R. YEALLAND.

THIS paper, which was based on observations made in one hundred cases of hysterical fits, over a period varying from two to seven years, dealt with the subject more from a physical than from a psychological aspect. The author pointed out that victims of hysterical fits can be made to reproduce a seizure by simple methods. In some cases a command to demonstrate the attack is all that is necessary; in others, considerable persuasion is needed. The patient's response to reproduce a seizure to order is considered to be of some diagnostic value, and it is employed as a suggestive factor in the plan of treatment he adopts, which consists in demonstrating to the patient during the seizure so reproduced that consciousness is retained throughout the attack.

The following classification of types of seizures was suggested: (1) An apparent momentary loss of consciousness. (2) A state of apparent coma lasting for hours in which the pulse and respiration rates are normal. (3) A pseudo-tonic convulsion. (4) A pseudo-clonic convulsion. (5) A convulsion beginning in the pseudo-tonic contraction and followed by a pseudo-clonic contraction. (6) Hystero-epilepsy. (7) Attacks of uncontrollable laughing or crying in which large quantities of urine are passed. (8) Other violent movements expressed in attempts to injure himself or those who attempt to restrain the patient by holding him down. (9) Attacks of staggering.

Illustration of each type of case was given, together with the treatment employed, and it would appear therefrom that the method of application varies somewhat in each case. It is one of suggestion and re-education. The percentage of recoveries from recurrence of attacks was given as sixty. Types 3, 6 and 7 were more difficult to treat, but even in them a marked reduction in the number of seizures was noted.

DISCUSSION.

The paper was discussed by Drs. Reynell, Patrick and Harris, who agreed that such methods as were advocated in it have often a considerable pragmatic value. Surprise was expressed that a larger proportion of permanent cures had not been obtained by the author.

Notices of Recent Publications.

Die Lehre vom Tonus und der Bewegung, zugleich systematische Untersuchungen zur Klinik, Physiologie, Pathologie und Pathogenese der Paralysis Agitans. Von F. H. Lewy. S. 673, mit 569 zum Teil farbigen Abbildungen und 8 Tabellen. Berlin: J. Springer. 1923. Price 40s.

It is mainly to the study of paralysis agitans that this large monograph is devoted, but in his effort to be as complete and comprehensive as possible the author has extended his work to many cognate subjects, as tonus and its chemico-physical basis, the physiology of the co-ordination and synthesis of movement, the development and structure of the corpus striatum, and the anatomy and physiology of the vegetative system. All these chapters are well worth reading, though some of them contain little new or striking in the matter of observation or in the explanation of function.

It is, however, those sections on the clinical and pathological aspects of Parkinson's disease that give the book its undoubted value. His observations on the pathology of the disease alone are based on the histological investigation of the central nervous system in sixty cases.

In the first chapter interest falls mainly on the careful study of the vegetative and psychical disturbances of paralysis agitans, and the conclusion that this disease is to be regarded as a pathological form of premature senility in which, however, the lesion falls on the centres of involuntary mobility and on the vegetative nervous system, rather than on the cortex.

There follows in the second chapter a lengthy analysis of movement by direct and indirect muscle tracings, and by the simultaneous recording of electrical changes in the agonists and antagonists by means of two string galvanometers, in various nervous disorders as well as in paralysis agitans. The special form and the significance of the various types of curves obtained in the latter disease are fully considered, and important conclusions as to the nature of the disturbances of nervous functions that they indicate are discussed.

The anatomy of the disease is also dealt with in a very complete and thorough manner. Structural changes are described in most parts of the nervous system, in the cerebral cortex where the frontal and temporal lobes suffer most, in the cerebellum and in the brain-stem, but the most essential are those that exist in the corpus striatum where cellular, interstitial and vascular changes occur more or less independently of one another. All these lesions are of an analogous nature of those found in senile and presenile degeneration, and their anatomical localization is to be explained, according to

the author, partly by the peculiar mode of distribution of the blood-vessels in the affected region, and partly by a primary affection of the liver, and perhaps, too, of some of the ductless glands, as the thyroid, which makes the corpus striatum and related parts of the nervous system more vulnerable to various pathological agents than they usually are.

Though certain of the author's conclusions may not be generally accepted, and though some of the arguments on which he bases them may become subjects of controversy, the volume must be regarded as a valuable contribution to the study of subjects on which much ignorance still exists. The manner in which the volume is published, and especially the reproduction of the numerous illustrations, deserves the highest praise.

Der amyostatische Symptomenkomplex. KlinischeUntersuchungen unter Berücksichtigung allgemein pathologischer Fragen. Von Dr. A. BOSTROEM. S. 205 mit 12 Textabbildungen. Berlin: J. Springer. 1922. Price 7s. 6d.

The title of this monograph is the term introduced originally by Strümpel to include disturbances of fixation of parts of the body owing to errors in the time or degree of the innervation of the muscles that subserve it, or to irregularities in their combinations. The clinical conditions which the author includes in it and describes here are idiopathic and symptomatic athetosis and chorea, progressive lenticular degeneration, pseudo-sclerosis and paralysis agitans, or rather Parkinsonism as a result of various structural affections of the brain. The clinical features of each of these conditions is carefully described and analysed, and in many instances are illustrated by the record of cases, especially by such as bring out special features or symptoms. The pathology of each is also discussed, especially in relation to the pathogenesis of the essential symptoms. The book is compact and readable, and will undoubtedly be of service in the study of these interesting diseases.

Die Lumbalpunktion. Dr. MARTIN PAPPENHEIM. Wien, Leipzig, München. Rikola Verlag. 1922. Pp. 184.

Books on the cerebrospinal fluid written by those familiar with the subject are still few, and therefore welcome. Dr. Pappenheim's book makes no pretence to open new ground, or even to cover the whole of the subject, but it is obviously written from personal experience and, so far as it goes, is a trustworthy guide to the examination of the cerebrospinal fluid. It is essentially a book of methods, and is more adapted to the needs of the laboratory worker than to those of the clinician. It deals particularly with the more chronic forms of nervous disease, and with the many special methods which have been devised for the diagnosis of the various syphilitic affections of the nervous system. Nearly ninety pages are occupied in the details of the examinations for cells, albumen and globulin, and with the colloidal gold and mastic,

Wassermann, Sachs-Georgi, and hæmolysin reactions. At the end of this we find that the differential diagnosis of general paralysis from other syphilitic diseases cannot be made on the results of any of these tests, either singly or in combination, but only on the alterations which take place in the reactions as the result of treatment. This conclusion is in agreement with the views of most modern authorities. The twenty pages on the diagnostic value of lumbar puncture are somewhat discursive, and many diseases are only incidentally mentioned. We miss a clear statement of the changes found in the cerebro-spinal fluid in each disease such as is given, for example, by Eskuchen. In fact, Pappenheim's book, either as a work of reference or as a laboratory handbook, cannot be compared with that of Eskuchen. It contains practically nothing new, and omits much valuable material that is given by the older books. It is, however, much shorter and more easily read. The bibliography is well arranged, and there is a good index.

The Form and Functions of the Central Nervous System; An Introduction to the Study of Nervous Diseases. By FREDERICK TILNEY and HENRY ALSOP RILEY. Second Edition. Pp. 1,019, with 591 figures, 56 of which are coloured. London: H. K. Lewis and Co. 1923. Price £2 12s. 6d.

The first edition of this book was reviewed in a previous volume of this Journal (1921, **44**, 90). The present edition is merely a reprint in which some typographical and a few other errors have been corrected. The authors assert that owing to the short time intervening since its first appearance, no radical changes in the text or illustrations are required, but it is none the less regrettable that some of those defects which were pointed out in the previous review, especially the absence of reference to other authorities on controversial points and the use of terms not generally accepted, should have remained unchanged.

Brain Abscess. By WELLS P. EAGLETON, M.D. Pp. 280. New York: The Macmillan Company. 1922. Price 31s. 6d.

This book, written chiefly from the standpoint of the otologist, consists of some 280 pages, of which number about a quarter are occupied with a review of a very large number of cases taken from the literature. The main part of the book, however, is based upon the author's personal experience of some fifty cases of abscess of the brain, and contains a good deal of interesting information. There are sections dealing with the surgical technique of intracranial operations, with the protective mechanism of the brain, and with the pathology and diagnosis of cerebral abscess. The author's method of dealing with such abscesses is given in much detail, but it is somewhat surprising to find no mention of enucleation of the entire abscess with its capsule.

Der Selbstmord. Dr. R. WEICHBRODT. Aus: Abhandlungen aus der Neurologie, Psychiatrie, Psychologie und ihren Grenzgebieten. Heft 22, S. 44. Berlin: S. Karger. 1923.

This small monograph is an interesting study on the problem of suicide from the historical, religious, sociological, philosophical and psychiatrical points of view. Statistics show that there are a greater number of suicides in large towns than in country districts; and that it is more common amongst the more educated classes, especially among those subjected to the stress of modern business. In the nineteenth century suicide was much more common in Europe in men than in women, in the proportion of four to one, but in the last few decades the proportion of female suicides has increased, especially in districts in which women have entered business and competition for livelihood. Religion has apparently little influence in checking suicide, in fact certain religions of the East and some of the American and African religions look upon suicide as a duty. The curve of suicide rises each spring, especially in the months of May and June, in every country.

Esquirol regarded suicide as invariably an act the result of psychopathic disturbances, but recently observers have paid more attention to external factors, as financial distress, threatened punishment, loss of friends, &c. Though these are undoubtedly important it is interesting that in many families there seems to be a hereditary tendency to suicide. Only a small proportion, forty to 1,400 suicides, of which a record has been kept in Berlin and Frankfort, have been previously confined in institutions owing to mental aberrations; among the insane the danger is greater at the beginning or end of the melancholic attack.

The only prophylactic measures that the author can suggest are careful education of psychopathic individuals, and confinement to institutions as soon as any signs of mental aberration appear.

Psychology and Morals: An Analysis of Character. By J. A. HADFIELD. Pp. 186. London: Methuen. 1923. 6s. net.

In the doubtful probability of man sacrificing the heritage that has been bequeathed to him by the great religious and moral systems of history, the change will take place only after long and painful struggles, compromises, and re-interpretations.

The book before us is an attempt to seize the most favourable moment for the development of the new psychology initiated by Freud and Jung. While accepting the hypotheses of the Freudian psychology for all working purposes, the author tempers the wind to the endurance of the shorn lamb by making a number of concessions to current moral ideas, in order that broad principles of the psycho-analytic position may be accepted without demur. But this does not weaken the force of the book, which is in the nature of a guide to the perplexed layman in his way through the labyrinth of new and somewhat terrifying ideas.

After an enunciation of the principles, Dr. Hadfield discusses the vexing problem of the will rather fully, for on this fulcrum the whole of the moral personality revolves. Dogmatism on this topic is unfortunately necessary in the interest of morality, but it leads to metaphysical difficulties. From this the author goes on to discuss the idealism which can only succeed if it springs from a unified personality in which all impulses are in equilibrium, and serves the moral ends of the individual. Knowledge of the self is necessary before the individual can achieve moral ends which will be in complete harmony with an integrated instinct and emotion-driven system. Psychological analysis alone will achieve this end, and by so doing will bring into harmony the impulses derived from lower strata of our natures.

The book bristles with difficulties born of the attempt to explain the lowest in terms of the highest, with the result that many of its dogmatic assertions would not bear investigation in the light of anthropology, or even in the light of a dispassionate study of the history of morals.

Behaviourism and Psychology. By A. A. Roback. University Bookstore, Harvard, U.S.A. 1923.

In the flood of literature from the United States on the subject of Behaviourism, Dr. Roback's book comes as a welcome and vigorous current in the reverse direction. It is an attempt on the broadest possible grounds to reassert the claims of psychology as an independent science; it is not, however, written in an apologetic strain but as though the author saw in attack the best method of defence.

The first part is historical, and traces the origin of the behaviouristic attitude in the work of Hobbes and Comte, and, in our own time, in the neo-realism foreshadowed in William James and fully developed by Dewey, Holt, Watson and others. The author's main objection on biological grounds is that it fails to give an adequate explanation of memory, and secondly, in all experimental investigations, however rigidly introspection may be ruled out, there must be "an injection of the experimenter's own introspection into the interpretation of the data."

In the second section he disposes of the behaviouristic claim to have ousted psychology from its position of lawgiver to the organic life: he does not, however, rest satisfied with his victorious assault but carries the battle on into the fields of ethics, jurisprudence, religion and sociology. "Are these studies possible in the light of Behaviourism?" he asks. Once having established the right of psychology to throw a light on organic life, it appears to follow logically that behaviourism will not apply to the more complex forms of activity.

The book, however, fails to do sufficient justice to the methodological value of behaviourism as an instrument of research. Although one may learn much from the observation of movements as response to stimuli, the significance of such activities is only to be understood by an interpretation of them in terms of ends and purposes. Purpose, however, is a category that has no application to

mechanism, and thoroughgoing behaviourism is mechanistic. No sooner is this category admitted than the laws of psychology, as apart from physiology, are *ipso facto* established as existing, although they may not be fully understood. With this established, psychology stands alone as an independent method of investigation and behaviourism takes its rightful place as a method also—a bridge between physiological concepts and mental concepts, and not, as it falsely claimed to be, a complete science and philosophy of the organism.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd. St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.